A DISSERTATION

ON

PROSPECTIVE STUDY OF SERUM FERRITIN AS A PROGNOSTIC MARKER IN A PATIENTS WITH DECOMPENSATED LIVER DISEASE

Submitted to

THE TAMILNADU DR. M. G. R. UNIVERSITY

CHENNAI

In partial fulfillment of the regulations

for the award of

M. D. DEGREE IN GENERAL MEDICINE

BRANCH I

GOVERNMENT MOHANKUMARAMANGALAM

MEDICAL COLLEGE, SALEM

MAY 2018

Government Mohan Kumaramangalam Medical College Hospital

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled **"PROSPECTIVE STUDY OF SERUM FERRITIN AS A PROGNOSTIC MARKER IN A PATIENTS WITH DECOMPENSATED LIVER DISEASE"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. V. SUNDARAVEL M. D.,** Professor, Department of General Medicine, Government Mohan Kumaramangalam Medical College Hospital, Salem, Tamil Nadu, India.

S. Sangeetha

Signature of the Candidate

DR. S. SANGEETHA

Date : October 2017

Place : Salem

Government Mohan Kumaramangalam Medical College Hospital.

CERTIFICATE BY THE GUIDE

This is to certify that this dissertation **"PROSPECTIVE STUDY OF SERUM FERRITIN AS A PROGNOSTIC MARKER IN A PATIENTS WITH DECOMPENSATED LIVER DISEASE"** is a bonafide work done by **Dr. S.SANGEETHA** in partial fulfillment of the requirement for the degree of M. D. in General Medicine, examination to be held in 2018.

Signature of the Guide

Dr. V. SUNDARAVEL M. D.
Professor,
Department of General Medicine
Government Mohan Kumaramangalam
Medical College Hospital
Salem, Tamil Nadu, India

Dr. V. SUNDARAVEL, M.D.,
Chief Civil Surgeon
Professor of Medicine
Govt. M.K. Medical College,
Hospital - SALEM - 1.
Reg. No. 41475

Date : October 2017

Place : Salem

Government Mohan Kumaramangalam Medical College Hospital

ENDORSEMENT BY THE HEAD OF DEPARTMENT

This is to certify that this dissertation **titled "PROSPECTIVE STUDY OF SERUM FERRITIN AS A PROGNOSTIC MARKER IN A PATIENTS WITH DECOMPENSATED LIVER DISEASE"** is a bonafide work done by **Dr. S.SANGEETHA** under overall guidance and supervision **of Dr.S.R. SUBRAMANIAN M.D.,D.Ch,** Professor and Head, Department of General Medicine, Government Mohan Kumaramangalam Medical College Hospital, in partial fulfillment of the requirement for the degree of M. D. in General Medicine, examination to be held in 2018.

Seal & Signature of the of the H.O.D

Dr. S. R. SUBRAMANIAN, M. D., D.CH
Professor & Head of the Department,
Department of General Medicine,
Government Mohan Kumaramangalam
Medical College Hospital Salem,
Tamil Nadu, India

PROFESSOR AND HEAD,
Department of Medicine,
Govt. Mohan Kumaramangalam
Medical College & Hospital,
SALEM - 636 001.

Date : October 2017

Place : Salem

Government Mohan Kumaramangalam Medical College Hospital

COPYRIGHT

I hereby declare that THE TAMILNADU DR. M. G. R. MEDICAL UNIVERSITY, CHENNAI, TamilNadu, India, shall have the rights to preserve, use and disseminate this dissertation/ thesis in print or electronic format for academic / research purpose.

S. Sangeetha

Date : October 2017

Signature of the Candidate

Place : Salem

DR. S.SANGEETHA

ACKNOWLEDGEMENT

I am extremely thankful to **Dr.P.KANAGARAJ, MD., Dean,** Government Mohan Kumaramangalam Medical College Salem, for allowing me to utilize the hospital facilities for doing this work.

I would like to express my heartfelt gratitude to my postgraduate mentor and teacher, **Dr.V.SUNDARAVEL M.D** Professor, Department ofGeneral Medicine, Government Mohan Kumaramangalam Medical College Hospital for his relentless encouragement and expert guidance throughout the period of the study and post graduate course. His enthusiasm and immense encouragement have been responsible for easing out many shortcomings during this work.

I am deeply indebted to **Dr.S R SUBRAMANIAN M.D. D.Ch,** Professor& HOD, Department of Medicine ,Government Mohan Kumaramangalam Medical College Hospital, for his fathomless enthusiasm and motivation throughout the study.

Warmest and sincere thanks to professors

Dr. S.SURESHKANNA M.D, Dr.D.VIJAYARAJU, M.D., DCH and Dr. M.MANJULA M.D, Dr. J.A.ELANCHEZHIAN M.D, for all the help, encouragement and guidance during my post graduation study period.

My warmest gratitude to **Dr. T. YOGANANDH M.D,** registrar, department of medicine for his guidance in completing the study. I would

like to express my gratitude to **Dr. V.RAJKUMAR M.D** and **Dr. P. ARUL M.D,** and Dr. **R.KARTHIKEYAN M.D.,** whose relentless encouragement inculcated in me a sense of confidence.

I am foever thankful **to Dr. KARTHIKEYAN M.D, DM in MGE.,** to choose this topic and for giving valuable guidance and suggestions during my study and thesis.

I am deeply grateful to all assistant professors in the department of general medicine for their immense help and guidance during my post graduation course.

I would like to acknowledge Mr. Venkatesh, for helping me to analyze and compile the statistical data for my study.

I extend my heartfelt thanks to all my colleagues and friends for their help rendered during my study.

I specially thank all my patients without whose cooperation this dissertation would never have seen the light of the day.

S. Sangeetha

Signature of the Canditate

Date :

Place : Salem

DR.S.SANGEETHA

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"PROSPECTIVE STUDY OF SERUM FERRITIN AS A PROGNOSTIC MARKER IN A PATIENTS WITH DECOMPENSATED LIVER DISEASE"** of the candidate ***Dr. S.SANGEETHA*** with registration Number **201511404** for the award of ***M.D.***, Degree in the branch of ***General Medicine.*** I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **1%** percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal

Dr. V. SUNDARAVEL, M.D.,
Chief Civil Surgeon
Professor of Medicine
Govt. M.K. Medical College,
Hospital - SALEM - 1.
Reg. No: 41475

PROFESSOR AND HEAD,
Department Of Medicine,
Govt. Mohan Kumaramangalam
Medical College & Hospital,
SALEM - 636 001.

Ref. No.6027/MEI/2015

Office of the Dean,
Govt. Mohan Kumaramangalam
Medical College, Salem – 30.

Dated: 26 .01.2016.

Ethical Committee Meeting held on 23.12.2015 at 11.00 A.M in the Seminar Hall, IInd Floor, Medicine Block, Govt. Mohan Kumaramangalam Medical College Hospital, Salem - 01.

Name of the Presenter with Address	Title	Name of the Guide and Address	Whether it is Approved or not.
Dr. S. Sangeetha, I Year, Post Graduate Student of MD (General Medicine), GMKMC, Salem-30.	"Prospective study on Serum Ferritin as a Prognostic Marker in a Patients with Decompensated Liver Diesease - 100 Cases in GMKMCH".	Dr. V. Sundaravel, MD., Associate Professor of General Medicine, GMKMC, Salem.	Approved

The Ethical Committee examined the studies in detail and is pleased to accord Ethical Committee approval for the above Post Graduate student of this College to carry out the studies with the following conditions.

1. She should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution to Government.

2. She should inform the institution Ethical Committee in case of any change of study procedure site and investigation or guide.

3. She should not deviate from the area of the work for which applied for Ethical clearance. She should inform the IEC immediately, in case of any adverse events or serious adverse reactions.

4. She should abide to the rules and regulations of the Institution.

5. She should complete the work within the specific period and if any extension of time is required she should apply for permission again and do the work.

6. She should submit the summary of the work to the Ethical Committee on completion of the work.

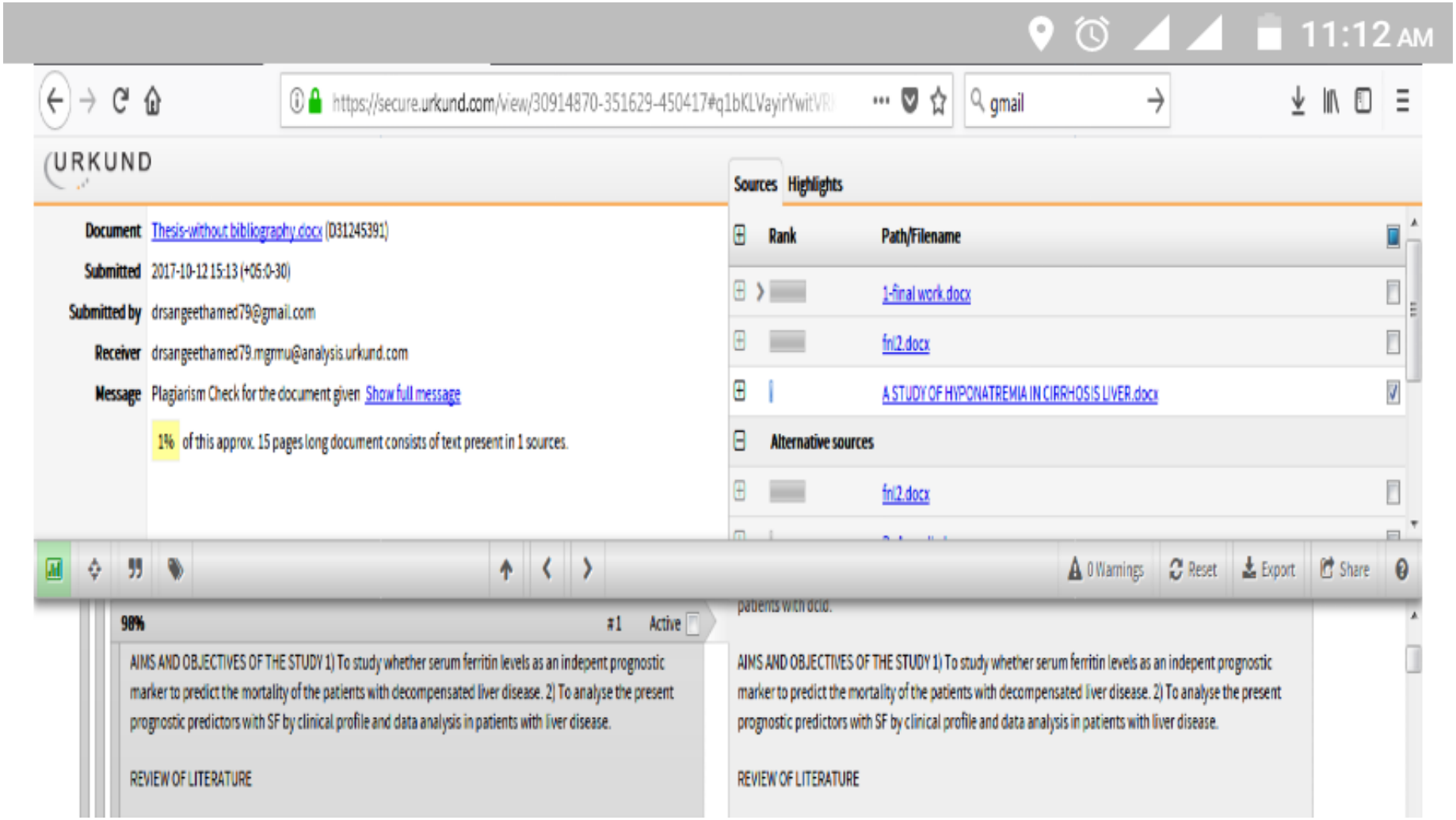
7. She should not claim any funds from the institution while doing the work or on completion.

8. She should understand that the members of IEC have the rights to monitor the work with prior intimation.

DEAN

6/1/16

To
The Individual.


11:12 AM
https://secure.urkund.com/view/30914870-351629-450417#q1bKLVayirYwitVR
gmail
URKUND
Sources
Highlights
Document Thesis-without bibliography.docx (D31245391)
Submitted 2017-10-12 15:13 (+06:0-30)
Submitted by drsangeethamed79@gmail.com
Receiver drsangeethamed79.mgmru@analysis.urkund.com
Message Plagiarism Check for the document given Show full message
1% of this approx. 15 pages long document consists of text present in 1 sources.
Rank
Path/Filename
1-final work.docx
fri2.docx
A STUDY OF HYPONATREMIA IN CIRRHOSIS LIVER.docx
Alternative sources
fri2.docx
0 Warnings
Reset
Export
Share
98%
#1
Active
AIMS AND OBJECTIVES OF THE STUDY 1) To study whether serum ferritin levels as an indepent prognostic marker to predict the mortality of the patients with decompensated liver disease. 2) To analyse the present prognostic predictors with SF by clinical profile and data analysis in patients with liver disease.
REVIEW OF LITERATURE
patients with acid.
AIMS AND OBJECTIVES OF THE STUDY 1) To study whether serum ferritin levels as an indepent prognostic marker to predict the mortality of the patients with decompensated liver disease. 2) To analyse the present prognostic predictors with SF by clinical profile and data analysis in patients with liver disease.
REVIEW OF LITERATURE

URKUND

Urkund Analysis Result

Analysed Document: Thesis-without bibliography.docx (D31245391)
Submitted: 10/12/2017 11:43:00 AM
Submitted By: drsangeethamed79@gmail.com
Significance: 1 %

Sources included in the report:

A STUDY OF HYPONATREMIA IN CIRRHOSIS LIVER.docx (D31101988)

Instances where selected sources appear:

1

ABSTRACT

BACKGROUND:

Decompensated liver disease caused by various modifiable and non modifiable factors leads to progression of cirrhosis, jaundice, bleeding varcies and other complications which leads to high complications and mortality.this study was carried out to predict whether serum ferritin a marker of body iron stores and inflammation is a valid prognostic marker in advanced liver disease.

MATERIALS AND METHODS :

It was a prospective and analytical study of 100 patients admitted in our hospital with dcld and its complications.the study period was from june 2016 to july 2017.after informed consent patients were evalvated with laboratory investigations, clinical examination.

INCLUSION CRITERIA;

1) Patients selected with referral to AASLD guidelines
2) Both male and female with chronic liver disease with decompensatation.
3) Around 35 to 60 yrs age groups were included

EXCLUSION CRITERIA

1) Age less than35 years and more than 60 years.
2) Prenatal women with liver disease.
3) Primary or secondary malignancy of liver

4) Patients is on hepatotoxic drugs

5) PLWHA

6) Chronic illness like tuberculosis.

RESULTS:

It was found that among enrolled 100 patients after getting informed consent, majority are male patients. but sex wise both female and male patients who are all showing high sf landed up with high mortality in the form of haematemesis with hypovolemic shock and hepatic encephalopathy.and also found that serum creatinin and hyponaterimia were independent important prognostic marker.By using Roche assay SF levels were calculated.normal limit for women was <200 ng/mi and for men <300ng/ml.most of the studied population had more than 400ng/ml.

CONCLUSION:

Serum ferritin is one of the surrogate marker to predict prognosis in the patients of dcld. compared with well estabilished prognostic model like MELD score ,to assess the mortality with SF level IS Statistically valid one. SO IN Future SF levels will be a one of the best screening independentt prognostic marker in people with liver disease.

KEY WORDS:

American Association for the study of liver disease, serum ferritin, decompensated liver disease.

TABLE OF CONTENTS

LIST OF FIGURES AND CHARTS

LIST OF TABLES

LIST OF CHARTS

LIST OF ABBREVIATIONS USED

ACLF	Acute on Chronic Liver Failure
APASL	Asia Pacific Association of Study of Liver
AASLD	American Association Study Of Liver Disease
DMT1	Divalent metal transporter 1
CTP	Child Turcott Pugh
CLD	Chronic liver disease
dcld	Decompensated liver disease
EASL	European Association of Study of Liver
INR	International Normalised Ratio
IL	Interleukin
MDF	Maddrey’s Discriminant Function
MELD	Model for End stage Liver Disease
HVPG	Hepatic vein pressure gradient
SBP	Spontaneous Bacterial Peritonitis
SF	Serum ferritin
HRS	Hepatorenal Syndrome
H.E	Hepatic Encephalopathy
HCC	Hepatocellular Carcinoma
HBV	Hepatitis B Virus

HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
AUDIT-C	Alcohol Use Disorders Identification Test
ALT	Alanine Amino Transferase
AST	Aspartate Amino Tranferase
GGT	Gamma GlutamylTransferase
PHG	Portal Hypertensive Gastropathy
UGI	Upper Gastrointestinal Tract
NAFLD	Non-Alcoholic Liver Disease
PT	Prothrombin Time
INR	InternationNormalised Ratio

INTRODUCTION

Chronic liver disease which will progress to cirrhosis indicate fibrosis of the liver. Patients with cirrhotic liver may presented with asymptamatic or compensated or else symptomatic or decompensated stage[(1)]. At any time due to various aggravating factor leads to acute decompensation on chronic liver failure occur with following Features :

Portal hypertension

Oesophageal varices

Ascites

Spontaneous bacterial peritonitis

Hepato renal syndrome

Hepato pulmonary syndrome

Hepatic encephalopathy

Above said terminology are already well defined by AASLD which guide us to predict the chances of high complications and death are common in decompensated stage only 18 month survival was 50% compared with compensated stage where the survival of 10 years was 50%.[(2)]

Data mining is used in our medical field to assess and correlate the prognostic markers to predict the mortality and time to decide for treatment like medical management or intervention like transplantation, emergency endoscopy band ligation etc.

By using correlation and regression analysis which is one of the valid statistical method guide to study the prognostic significance of the studied one.

Well studied prognostic model MELD score[2] is one of the mathematical model helps to know the outcome who are all underwent TIPS.

Correlation analysis helps us to assess linear relationship between two variables.[3]

In advanced liver disease with decompensation only curative therapy is liver transplantation. By using meld score we predict the prognosis and planned for further approach like transplantation.

Our study was carried out whether serum ferritin is efficient to predict the future outcomes in patients with dcld.

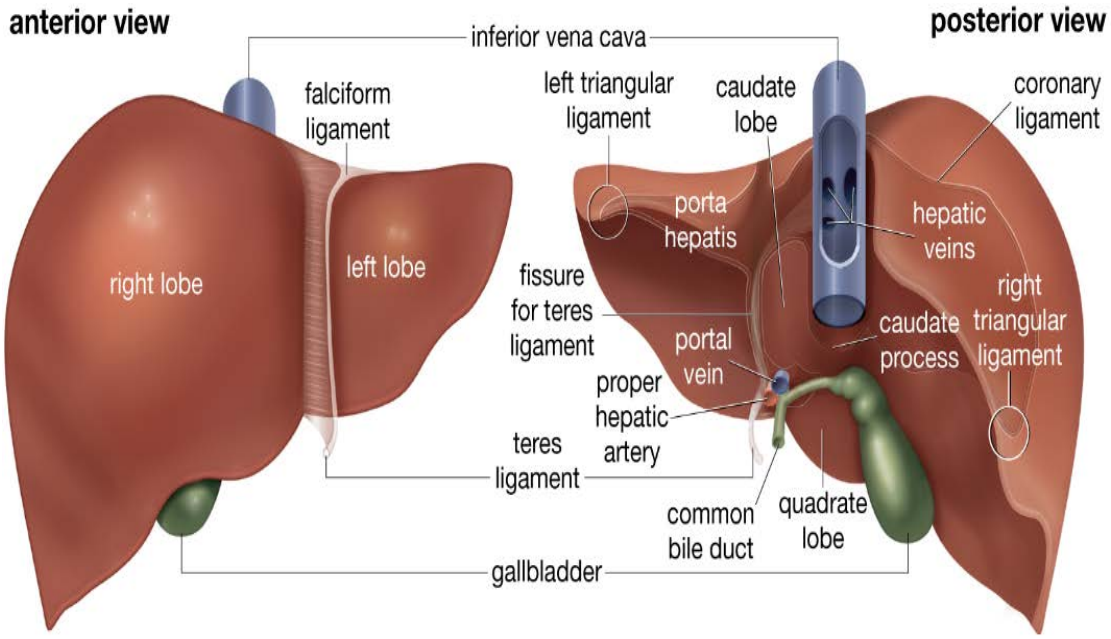
AIMS AND OBJECTIVES OF THE STUDY

1) To study whether serum ferritin levels as an indepent prognostic marker to predict the mortality of the patients with decompensated liver disease.

2) To analyse the present prognostic predictors with SF by clinical profile and data analysis in patients with liver disease.

REVIEW OF LITERATURE

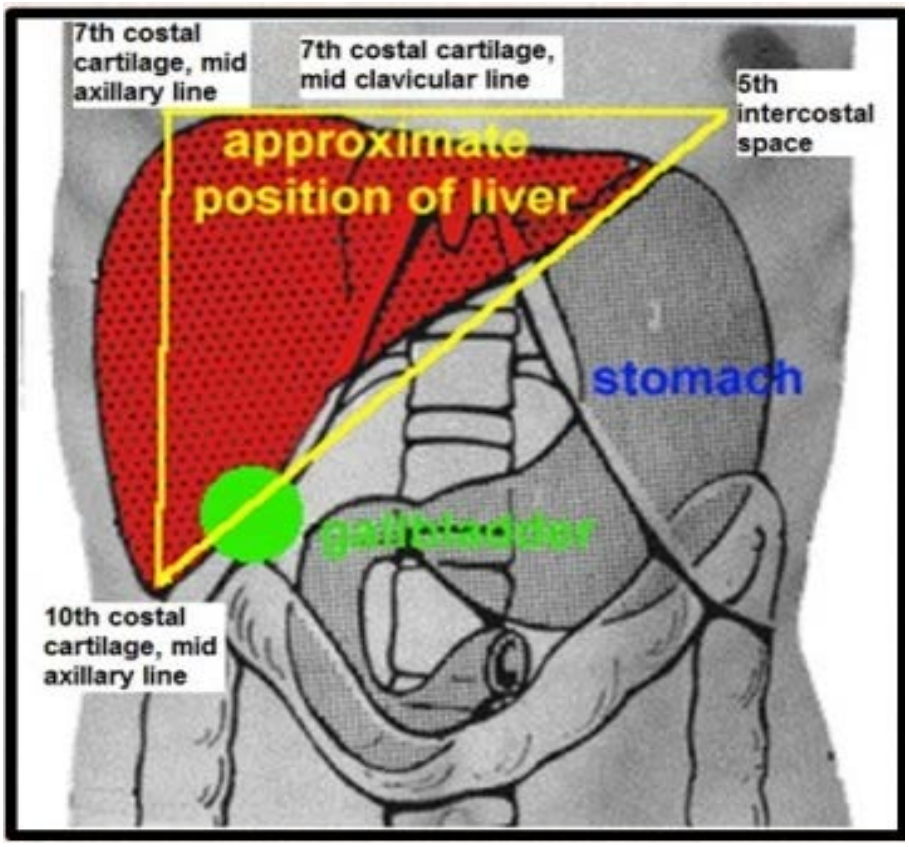
LIVER ANATOMY (FIGURE-1)



- Liver is Largest organ in our system
- Weight is around 1.4 gms in women to 1.8 gms in men[4,5,)]
- Divided in to two major and minor lobes
- By portal vein functionally divided in to eight lobes.
- Main functions of liver is to filter the blood, detoxifies chemicals, and Metabolizes drugs.

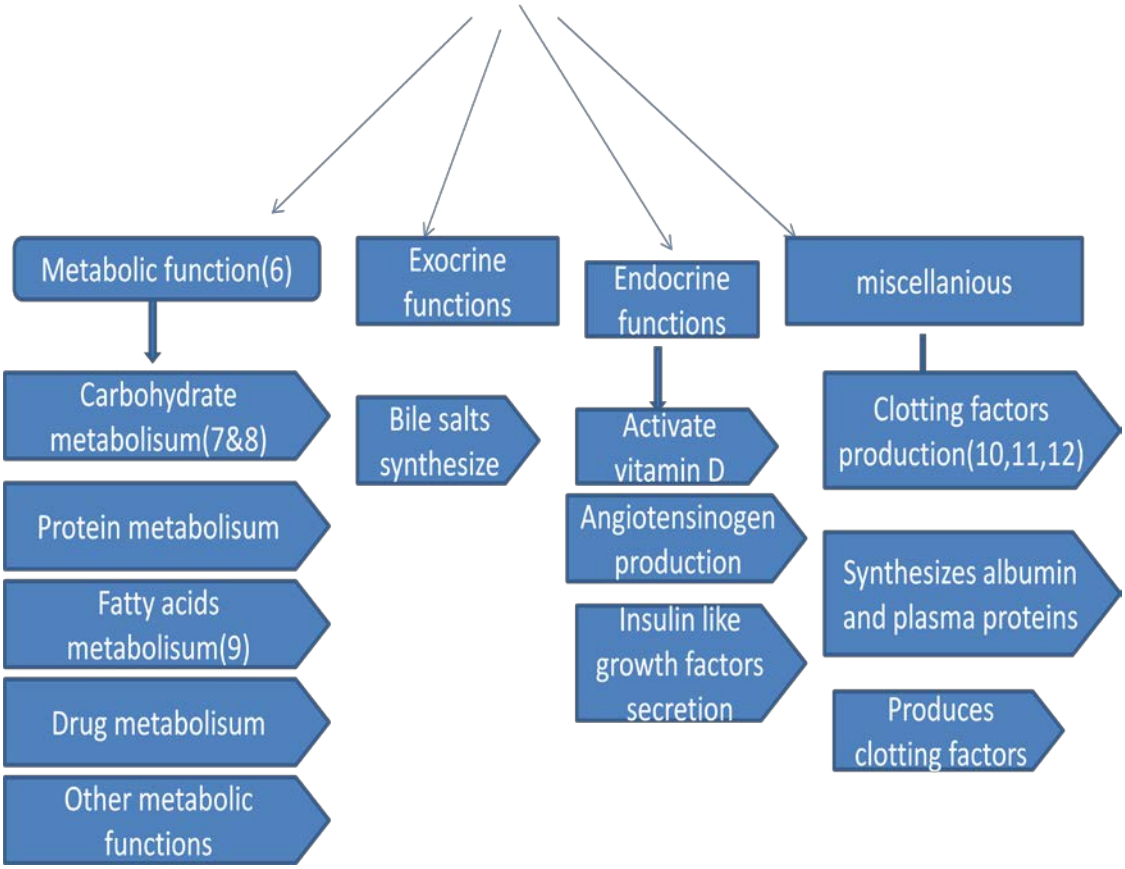
Liver produce proteins which is important for blood clotting and other functions.

SURFACE ANATOMY OF LIVER (FIG-2)



- Liver situated in right upper hypochondrium
- Extends from right 5^{th} intercostal space in mid clavicular line.
- Right lobe Upper border; 2cm medial to MCL at the level of 5^{th} rib.
- Left lobe UB ; at the level of 6^{th} rib in left MCL
- Lower border passes obliquely upwards from 9^{th} rib to 8^{th} left costal cartilage

FUNCTIONS OF LIVER(FLOW CHART-1)



Above flowchart showing functions of liver. It is an essential organ that producing proteins ,manufacturing cholesterol and triglycerides, glycogen synthesis ,and bile production.

Liver playing important vital role in our body to detoxifying ammonia which is a byproduct of protein metabolism into urea and excreted in urine by the renal system.

LIVER DEPENDENT VITAMINS-FAT-SOLUBLE VITAMINS(13)

TABLE-1

Vitamin	Function	Associated Abnormalities in Patients with Liver Disease
A	Activator of gene expression by RXR and RAR transcription factors. Important for embryonic development and regulation of adult genes	Vitamin A toxicity can lead to microvesicular fat, cirrhosis; hepatotoxicity potentiated in alcoholic liver disease
D	Regulation of calcium and phosphate homeostasis	Rickets caused by vitamin D deficiency in childhood cholestatic diseases
K	Posttranslational gamma-carboxylation of glutamic residues in coagulant and anticoagulant pathways and osteocalcin	Cholestatic liver disease can lead to fat malabsorption and vitamin K deficiency
E	Antioxidant residing in cellular membranes throughout the body	Chronic cholestatic syndromes can lead to secondary neurologic impairment due to long-standing vitamin E deficiency; mutations in cytosolic tocopherol-binding protein associated with selective vitamin E deficiency

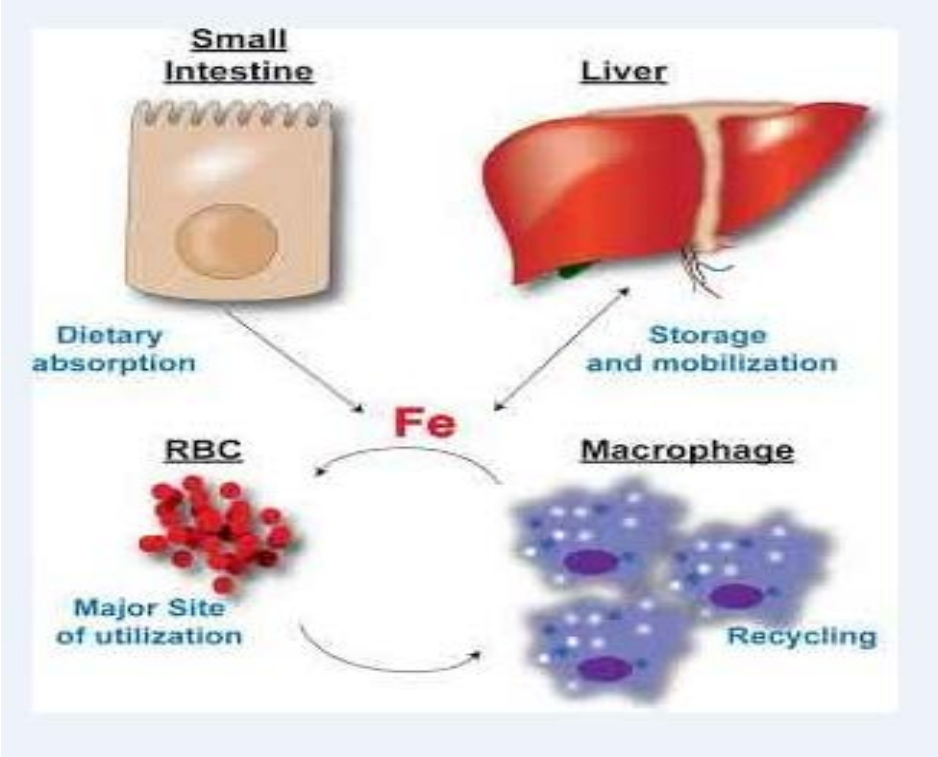
* RAR, retinoid alpha receptor; RXR, ligand-dependent transcription factor.

- Bile acids are essential for absorption of fat soluble vitamins which depends on normal liver cell function.[13].
- Vitamin A is essential for vision, immune system, growth of bone and reproductive system which is stored liver.
- Vitamin D which is not only important for strengthen of skeletal system also important for immune function and reduce inflammation.
- Vitamin E acts as an antioxidant and boosts our immune system.
- Vitamin K is important for clotting of blood .some of the enzymes in coagulation pathway is also dependent on vitamin k.
- In liver cell failure either acute or chronic patients more prone for deficiency of fat soluble vitamins. especially vitamin k. So measurement of serum PT (Prothrombin Time) is important.

- Prolonged PT(INR >3) along with normal fibrinogen concentration and normal platelets are highly indicate vitamin K deficiency.

NORMAL IRON STORAGE AND METABOLISUM

FIGURE-3



- Iron stored in tissues as ferritin and hemosiderin
- As transferrin in blood
- Excess fe stored as ferritin form in liver, bonemarrow and also in spleen.
- 23% of iron stored as ferritin.
- Absorption of dietary iron from duodenum is an important role in homeostasis of iron in the body.

- Around 1 to 2 mg of dietary iron absorbed by our body and balanced with losses like menstruation, sloughed intestinal mucosal cells.
- Iron distributed between haemoglobin, muscle, liver and macrophages.

IRON STORAGE AND FUNCTIONS

- We know one of the essential micro nutrient in our body is iron.

Uses :

1) HB SYNTHESIS

2) OXIDATION-REDUCTION REACTION

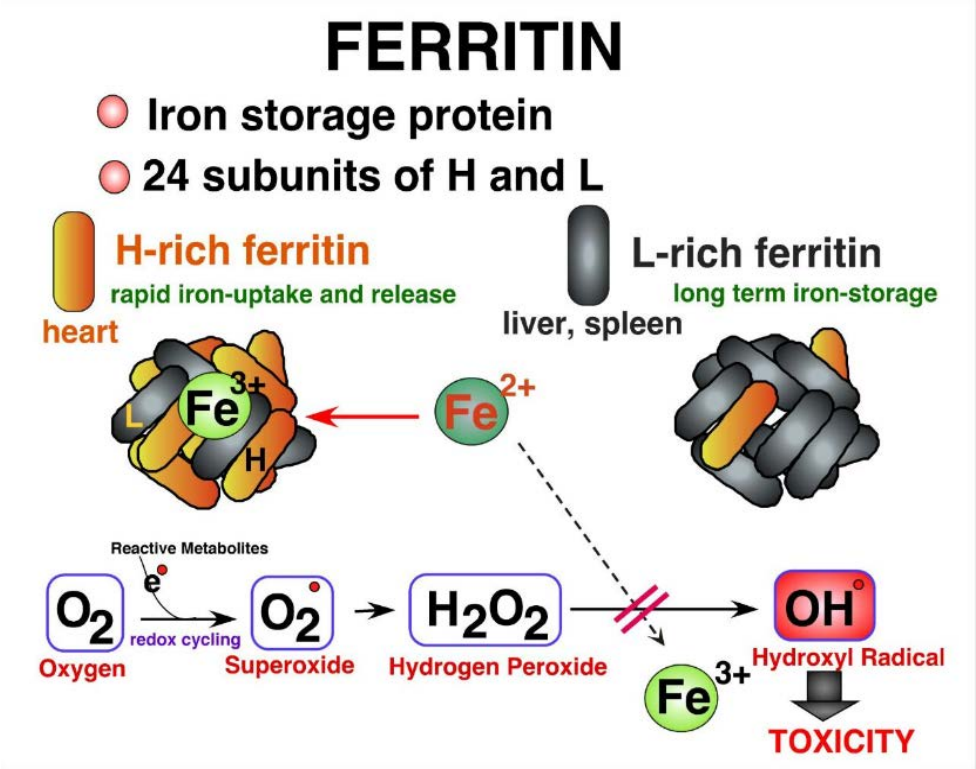
3) PROLIFERATIONS OF CELLS

4) and synthesis of cytocrome oxidase, peroxidase, and catalase.

   - Iron plays vital role in cellular metabolism and aerobic respiration. So overload of iron inside the cells leads to production of free radicals and lipid peroxidation which causes cell death.
   - Since liver is an important storage organ for iron. Overload of iron results in progressive injury to the liver cell and eventually leads to cirrhosis and hepatocellular carcinoma.

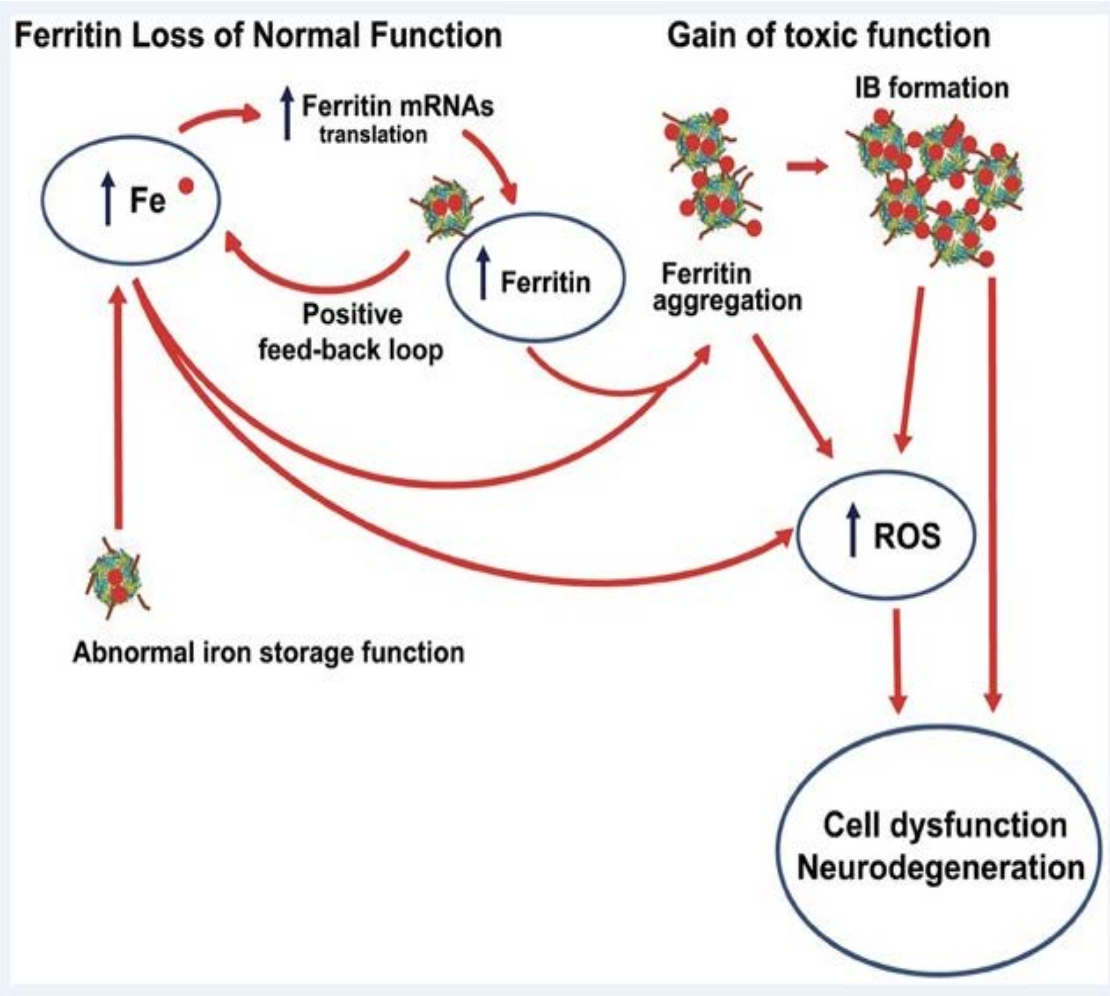
BELOW FIG- 4

SHOWS THE EXCESS TOXICITY OF FERRITIN



- Iron in association with ferritin stored in all cells.
- From ferritin To release of iron needs reduction of[14]
- Fe+3(ferric), Fe +2(ferrous form)
- (apical ferric reductase duodenal cytochrome b)
- (apical iron transporter DMT1)
- oxidised back to ferric
- form(Fe +3)

BUT EXCESS IRON LEADS TO DYSFUNCTIONS OF ORGANS BY PRODUCING ROS. (FIG-5)



Above figure clearly explains how iron overload inside the cell leads disturbed iron homeostasis and causing cell toxicity by ROS .

CIRRHOSIS AND ITS CO-FACTORS

Various co- factors like age, sex, duration may lead to progression of disease.

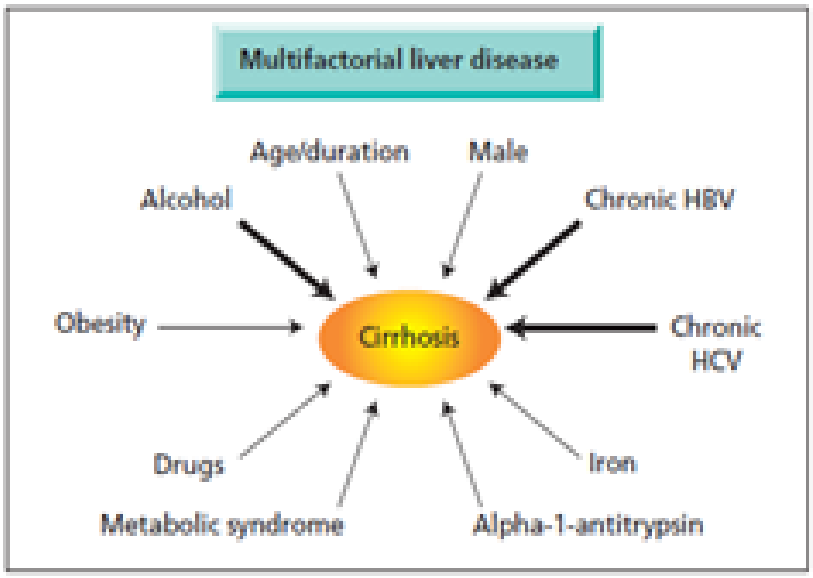


FIGURE 5.1

Even though alcohol is the main cause of cirrhosis in india there is lots of cause for cirrhosis.

All the above causes shown in figure leads to iron overload of liver cell and damage which ultimately leads to increased ferritin levels in serum.

Basic pathology what we understood was infectious cause,inflammatory cause,or alcoholism,metabolic all disturb the iron homeostasis and leads to liver injury.

RENE LAENNEC(FIG-6)

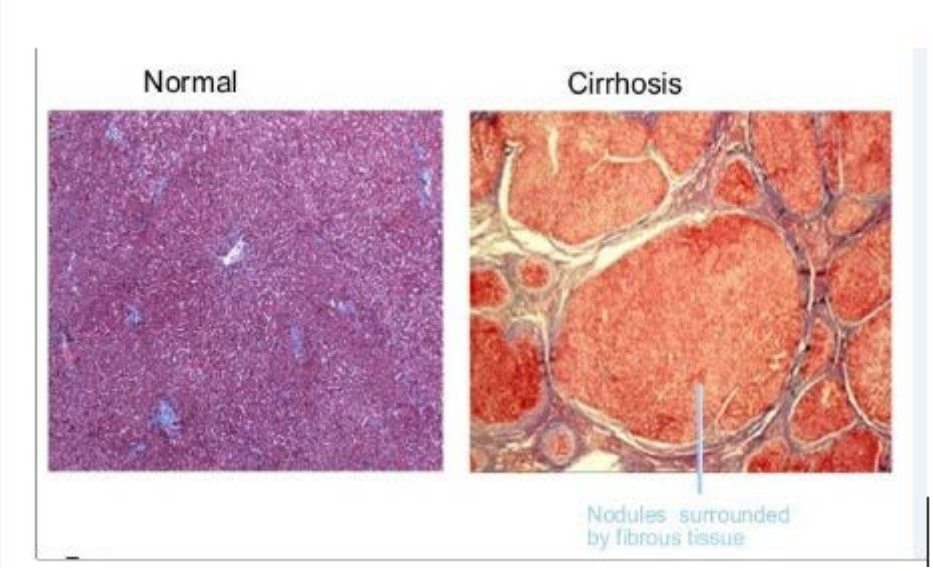
CIRROSHSIS DEFINITION

- In 1826 laennec coined the name cirrhosis.
- From greek word schirrous which denotes tawny surface of the liver derived the name cirrhosis.
- It is defined as histological evidence of fibrosis with regenerative nodules.
- Working group classification by WHO, define it's a diffuse process of normal liver architechture replaced by structurally abnormal nodules[15] and fibrosis.

HISTOLOGIC FEATURES OF NORMAL AND

CIRRHOTIC LIVER

(FIG-7)

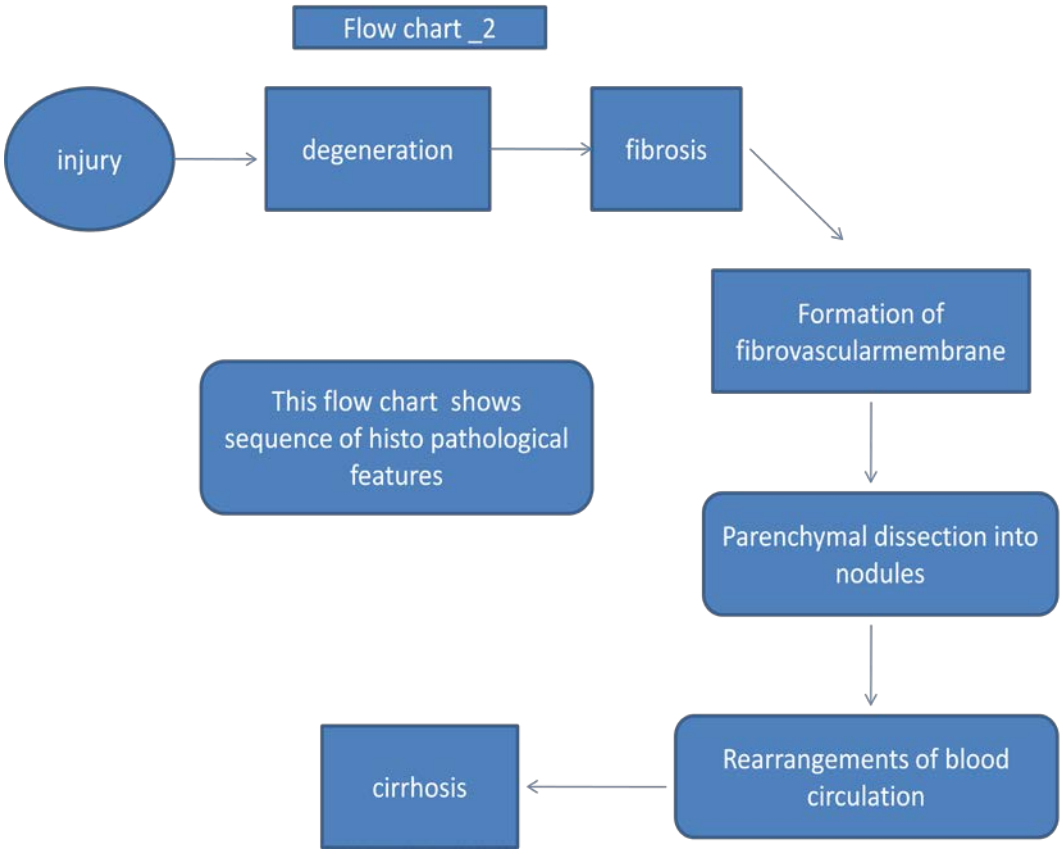


Above histology clearly shows regenerative nodules with cirrhosis.

HISTOLOGY OF CIRRHOSIS FEATUERS ARE

Microscopically regenerative nodules are present in hepatocytes and

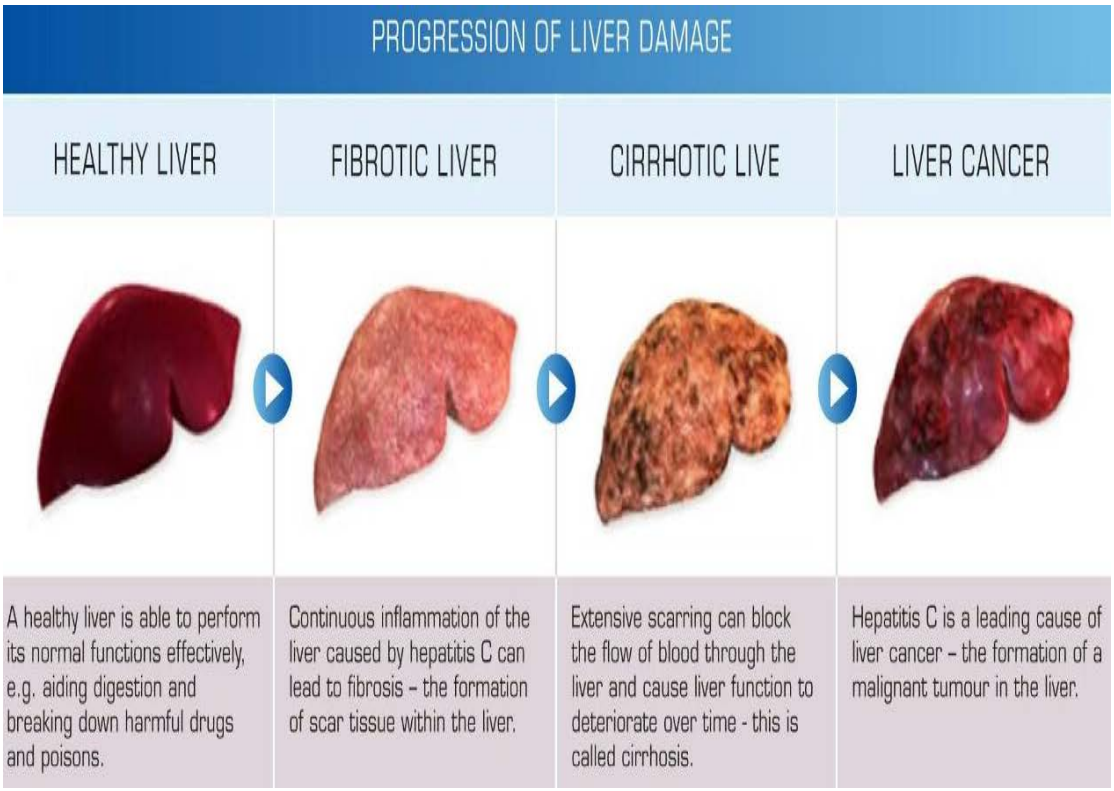
Showing fibrous connective tissue which connects like bridges between portal tracts.



Above flow chart (2) gives us the information regarding sequence of injury of the liver cell by iron overload and subsequent progression of fibrosis, degenerative nodules and cirrhosis.

BELOW FIG SHOWS PROGRESSION OF LIVER DISEASE

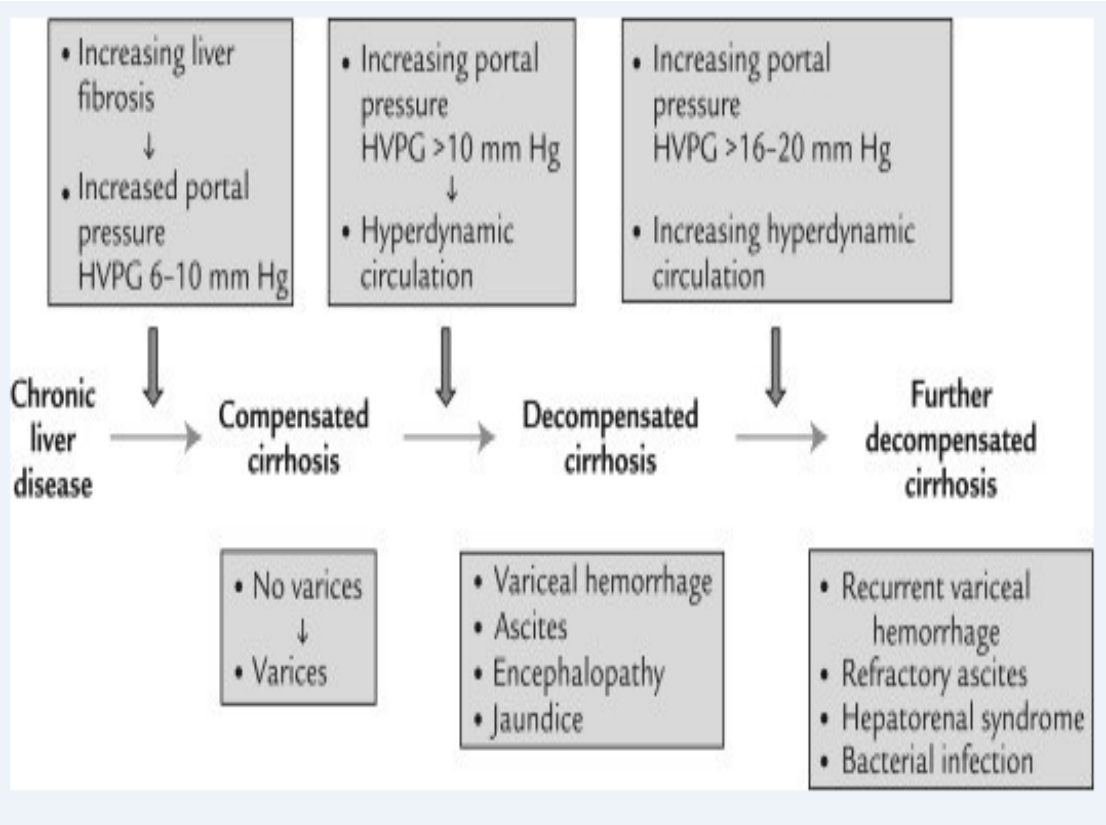
(FIG-8)



Above morphology of liver shows progression of liver damage .

Here the cause of iron overload is hepatitis c which is one of the leading cause for hepatocellular carcinoma.

FLOW CHART -3



Above flow chart helps us conclude how chronic liver disease progressed to compensated and decompensated cirrhosis and its complications.

Table-2

ETIOLOGY	TREATMENT
Ethanol related	Counseling &**Abstinence**
NASH	Reduction of weight,healthy food habits
Virus related eg: hep B,c&D	Treat with antiviral drugs.
hemochromatosis	venesection
Wilsons disease	Copper chelator therapy
Deficiency of α 1 - antitrypsin	Transplantation of liver
Primary biliary cirrhosis	Liver transplant
Iron overload status	venesection
Veno occlusive disease-budd chiari syndrome	Remove the venous block.final option is replacement of liver.
Galactosaemia	Avoid milk products and milk
Cardiac cirrhosis	Treat the failure heart
Auto immune hepatitis	Immuno suppresive drugs
Hepato toxic drug induced	Stop the drugs
Primary sclerosing cholangitis	transplant
Tyrosinaemia	Tyrosine free diet
Type IV glycogenesis	transplantation

Above table-2 shows various etiology of cirrhosis and treatment

WHO CLASSIFICATION OF CIRRHOSIS (FLOW CHART-4)

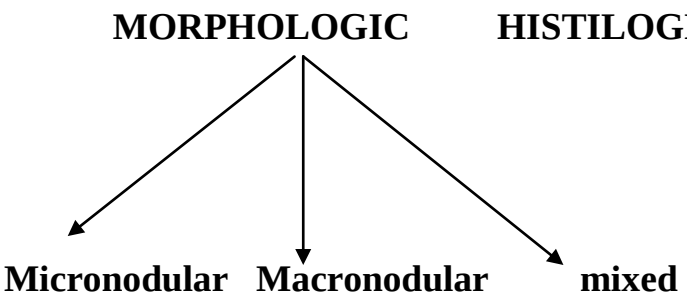
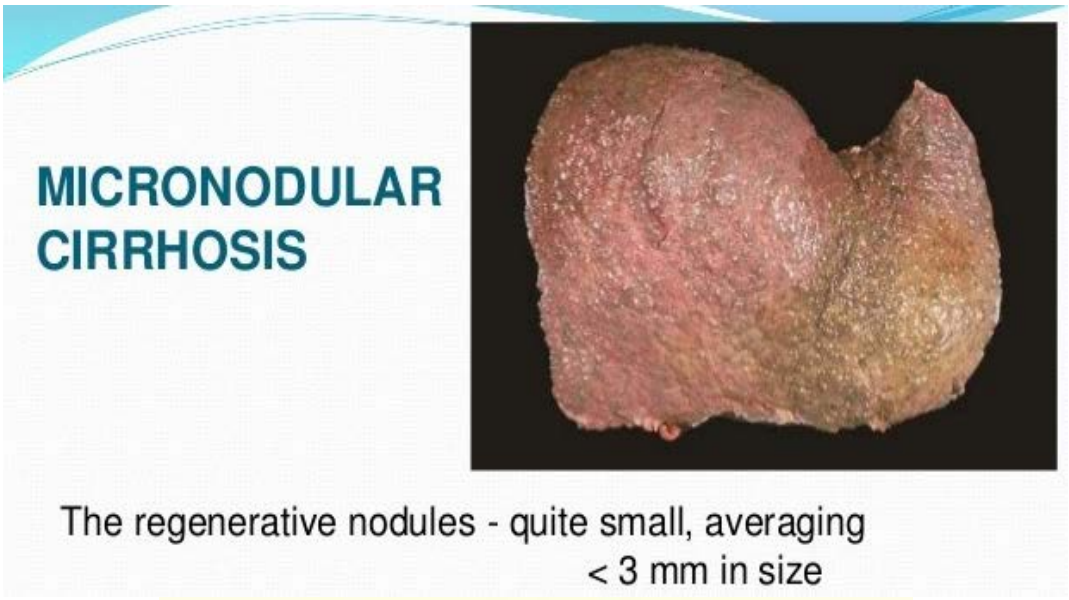
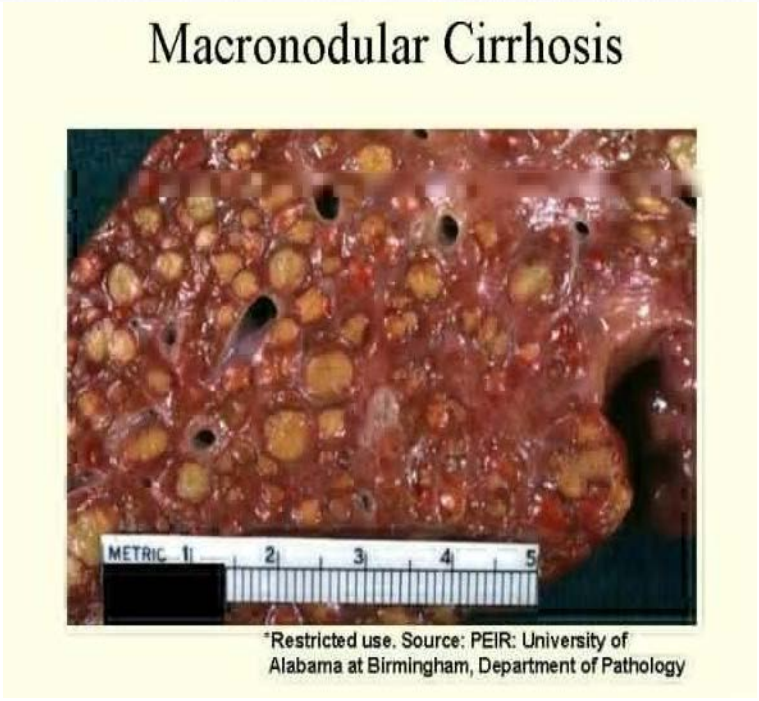


FIGURE 8.1





HISTOLOGIC

1) Portal

2) Post necrotic

3) Posthepatitic

4) Biliary

5) Congestive

ETIOLOGIC

1) Genetic

2) Toxic

3) Infectious

4) Biliary

5) Vascular

6) cryptogenic

MORPHOLOGICAL CLASSIFICATION

Size of liver

1. Normotrophic cirrhosis
2. Hypertrophic cirrhosis
3. Atrophic cirrhosis

Size of regeneration

1. Fine-nodular (granular) cirrhosis
2. Coarse-nodular (nodular) cirrhosis
3. Coarse-bulbous (lobular) cirrhosis
4. Mixed-nodular cirrhosis
5. “Smooth” cirrhosis

Structure of the fine tissue 1. Multilobular (multiacinar) cirrhosis 2. Monolobular (monoacinar) cirrhosis 3. Mixed forms
Progression of cirrhosis 1. Active (progressive) form 2. Inactive (stationary) form
Completion of cirrhosis 1. Complete form 2. Incomplete form 3. Incomplete septal cirrhosis

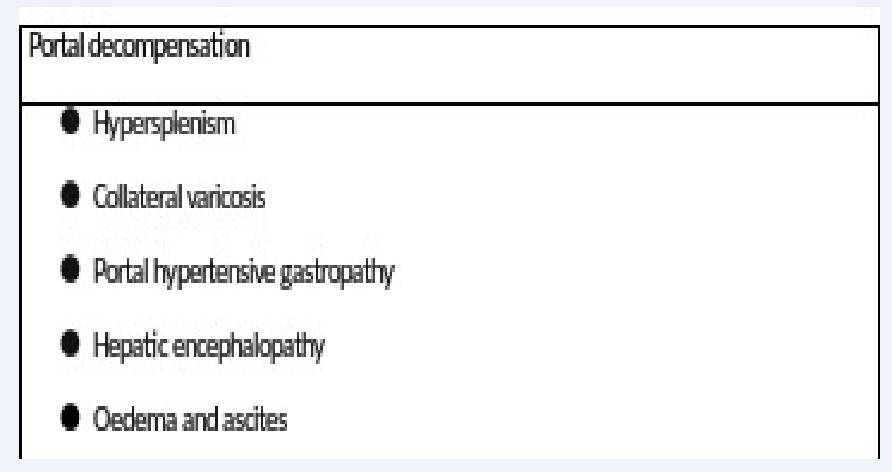
APPROACH OF CIRRHOSIS

Compensated liver disease;

Patient may have Asymptomatic varices , But do not have symtoms

Decompensated liver disease:

- Patients with symptom with life thretaning complications and presented with ascites, variceal hemorrhage, encephalopathy, jaundice.
- Decompensation have two forms either metabolic or portal decompensation.



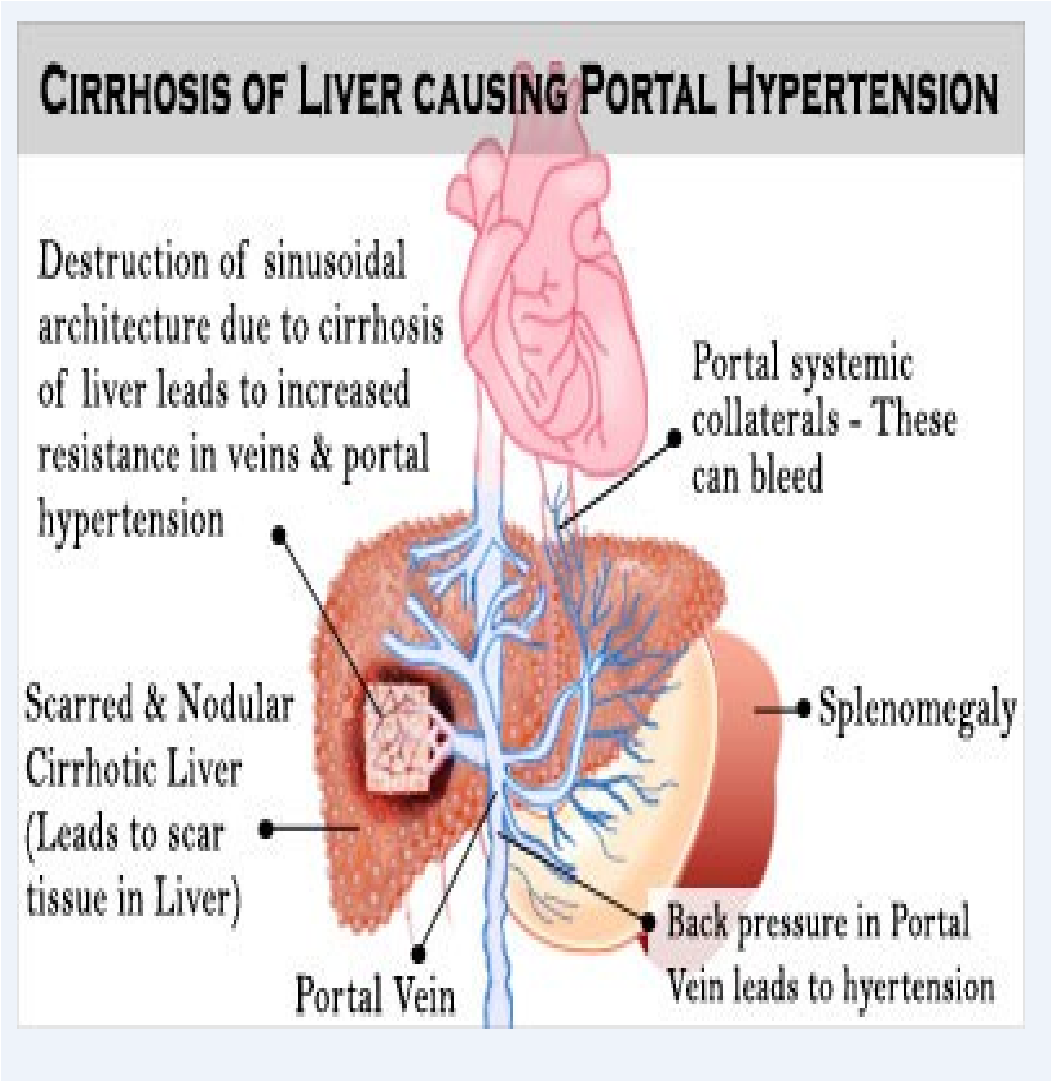
Metabolic decompensation
Jaundice • Encephalopathy • Oedema, ascites • Disturbed coagulation • Impaired protein and carbohydrate metabolism • Disturbed biotransformation • Hormonal dysbalances • Altered pharmacokinetics • Bacterial and viral infections • States of deficiency

Etiology and Pathophysiology of Portal Hypertension

Normal Liver Blood Flow

Hepatic blood flow is normally about 1500 mL/minute, epresenting 15% to 20% of cardiac output.

One third of this flow and 30% to 60% of the oxygen consumed by the liver are provided by the hepatic artery.



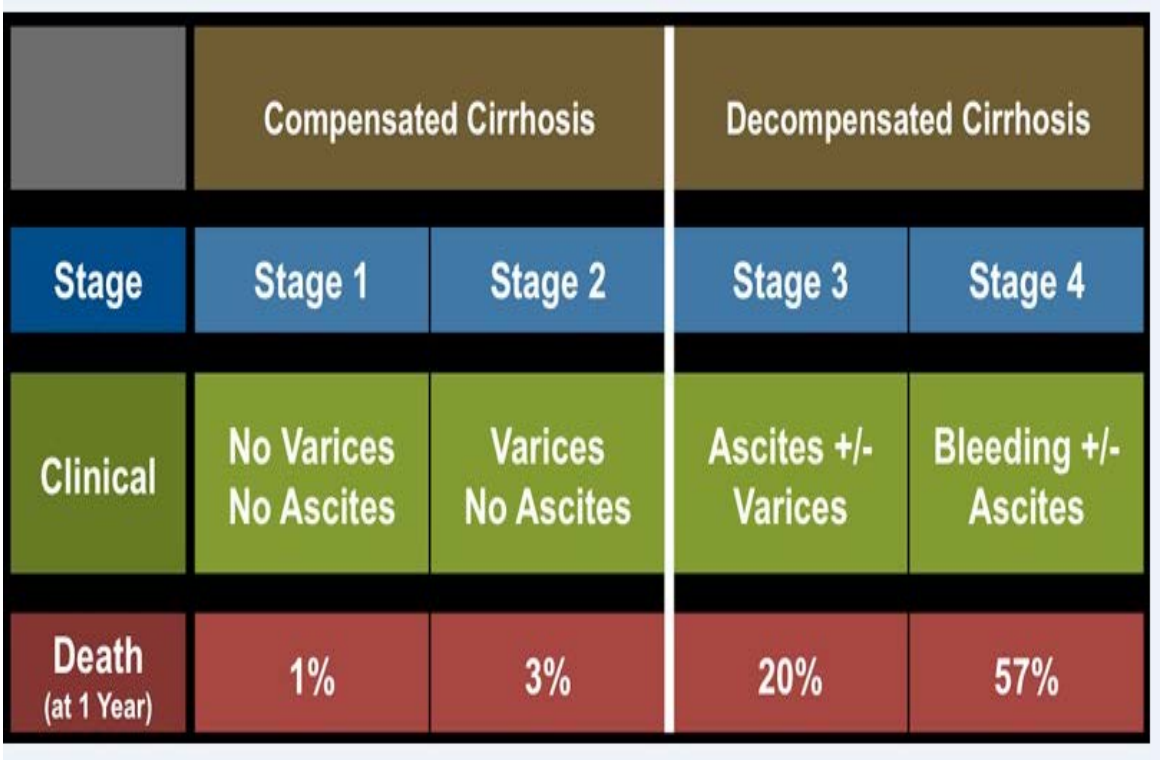
ABOVE FIGURE 8.2 SHOWS CIRRHOSIS OF LIVER PROGRESSION IN TO PORTAL HYPERTENSION

In portal hypertension, perfusion of the liver by portal blood is decreased and may be negligible. In approximately 10% of patients, flow within the portal vein may even be reversed (retrograde or hepatofugal portal flow).

This situation develops when hepatic arterial blood flow encounters greater resistance to flow in its usual anterograde course through the sinusoids than via the path offered by the portal venous radicals backward to the portal venous circulation. This loss of hepatic arterial blood flow, or hepatic arterial steal, via collaterals is associated with a highrisk of impaired hepaticfunction and hepatic encephalopathy.

CLASSIFICATION SYSTEM OF FOUR STAGE CIRRHOSIS (16)

TABLE-3



	Compensated Cirrhosis		Decompensated Cirrhosis	
Stage	Stage 1	Stage 2	Stage 3	Stage 4
Clinical	No Varices No Ascites	Varices No Ascites	Ascites +/- Varices	Bleeding +/- Ascites
Death (at 1 Year)	1%	3%	20%	57%

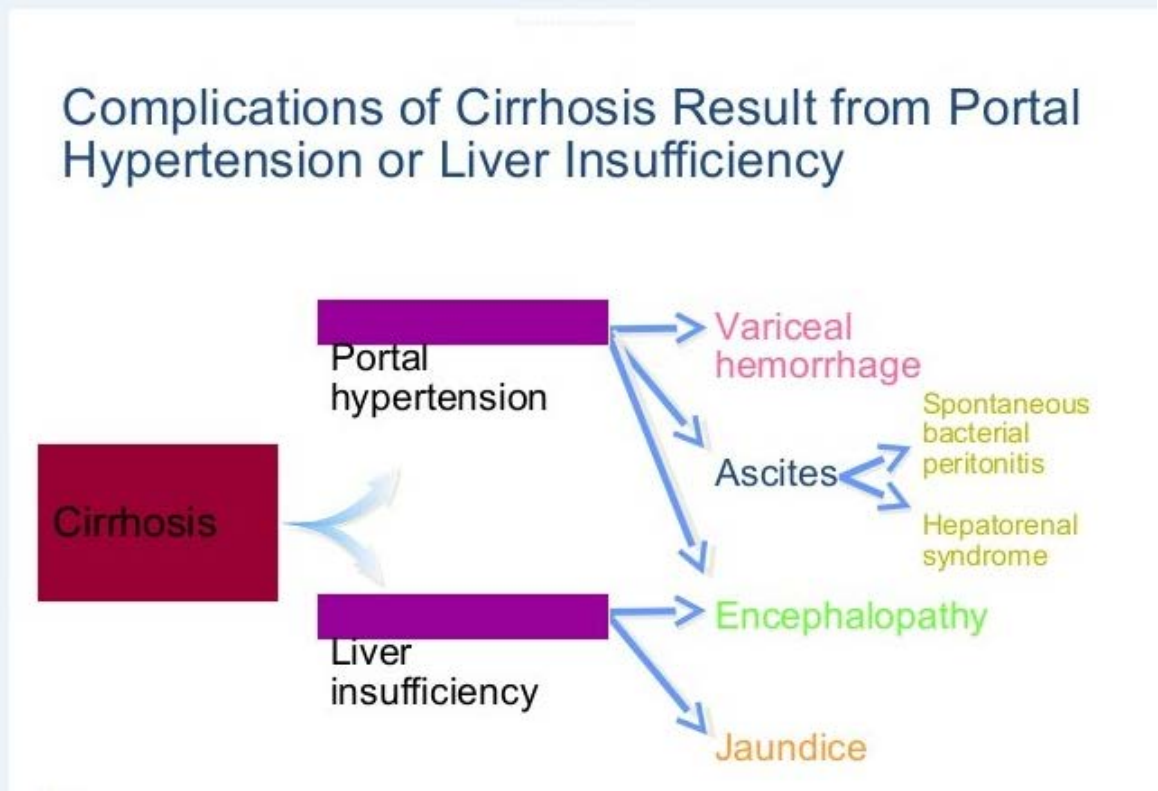
- Pts with stage 1&2-compensated[16]
- Stage 3&4 -decompensated

PROGNOSIS DECIDING FACTORS IN CLD

- Death in liver disease mainly due to decompensation of liver cell functions.
- PHT Plays a crucial role in patho physiology in cirrhosis.
- If HVPG >10 mmhg , having tendency to develop esophageal varices.
- If HVPG > 12 mmhg,more prone to develop bleeding from varices.
- With using Hepatic venous pressure gradient
- We will assses the chances of patient to develop varices.[17]
- If HVPG >10 mmhg the average time for the patients prone for variceal bleeding is around 4 years[18] bleeding from varices directly proportionate to the size of varices which related to high mortality[17,18,19,)]

FLOW CHART-5

Below flow chart showing complications of portal hypertension.



Complication of cirrhosis include edema, ascites, spontaneous bacterial peritonitis, bleeding from varices, hepatic encephalopathy, hepatorenal syndrome, hypersplenism, and liver failure.

INCIDENCE OF DECOMPENSATION

- Most common decompensating event in cirrhotic patients is ascites followed by variceal bleeding, jaundice, hepatic encephalopathy.[20]
- Decompensate occur 5% per year(20) in cirrhotic patient.
- In pts with esophageal varices incidence increases twice compared with not affected with varices.
- While cirrhosis often progresses undetected until a patient develops signs of decompensation, there are physical examination findings that suggest development of portal hypertension.
- Portal hypertension is defined as the elevation of hepatic venous pressure gradient above 5mmhg.
- Gastro oesophageal varices form when the development of portal hypertension necessitates an alternative route for blood to return from the portal system to the systemic circulation.
- Hepatic encephalopathy and most common, manifestation ascites are complications of portal hypertension.

PREDICTING FACTORS FOR DCLD

- MELD SCORE[21]
- HVPG>10mmhg[21]porta
- High BMI[23]

MELD SCORE

- MELD = 3.8(SERUM BILIRUBIN –MG/DL)+11.2 IN INR + 9.6 IN SERUM CREATININE – MG/DL+ 6.4

PHT AND ASCITES

- The word ascites derived from greek and represent the meaning –bag
- Theories for ascites are;

    1) overflow

    2) underfilling

    3) recent theory is hypothesis of arterial vasodilatation of splanchnic circulation which includes both above theories.

The *serum-ascites albumin gradient (SAAG)* has been proved in multiple studies to categorize ascites better than either the total protein concentration or other parameters do .

The SAAG is based on oncotic-hydrostatic balance. Portal hypertension results in an abnormally high hydrostatic pressure gradient between the portal bed and asciticfluid

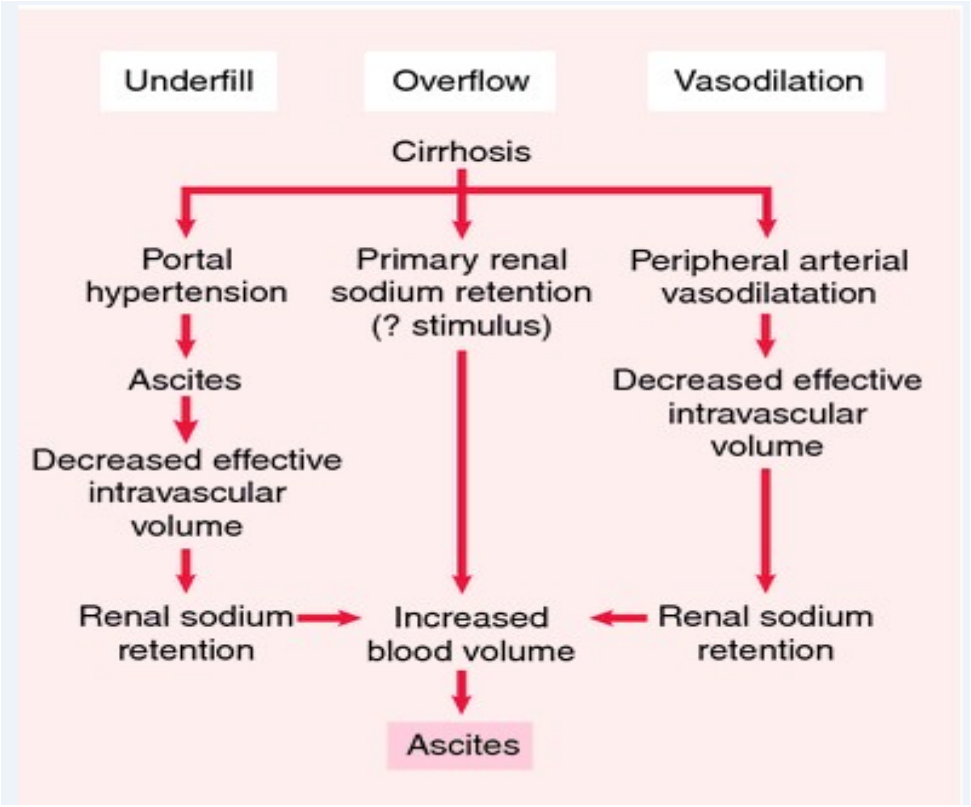
High Gradient 1.1 g/dL (11 g/L)	Low Gradient <1.1 g/dL (11 g/L)
Cirrhosis	Peritoneal carcinomatosis
Alcoholic hepatitis	Tuberculous peritonitis
Cardiac ascites	Pancreatic ascites
Mixed ascites	Bowel obstruction or infarction
Massive liver metastases	Biliary ascites
Fulminant hepatic failure	Nephrotic syndrome
Budd-Chiari syndrome	Postoperative lymphatic leak
Portal vein thrombosis Veno-occlusive disease Myxedema Fatty liver of pregnancy	Serositis in connective tissue diseases

Classification of Ascites by Serum-Ascites Albumin Gradient

(TABLE;3.1)

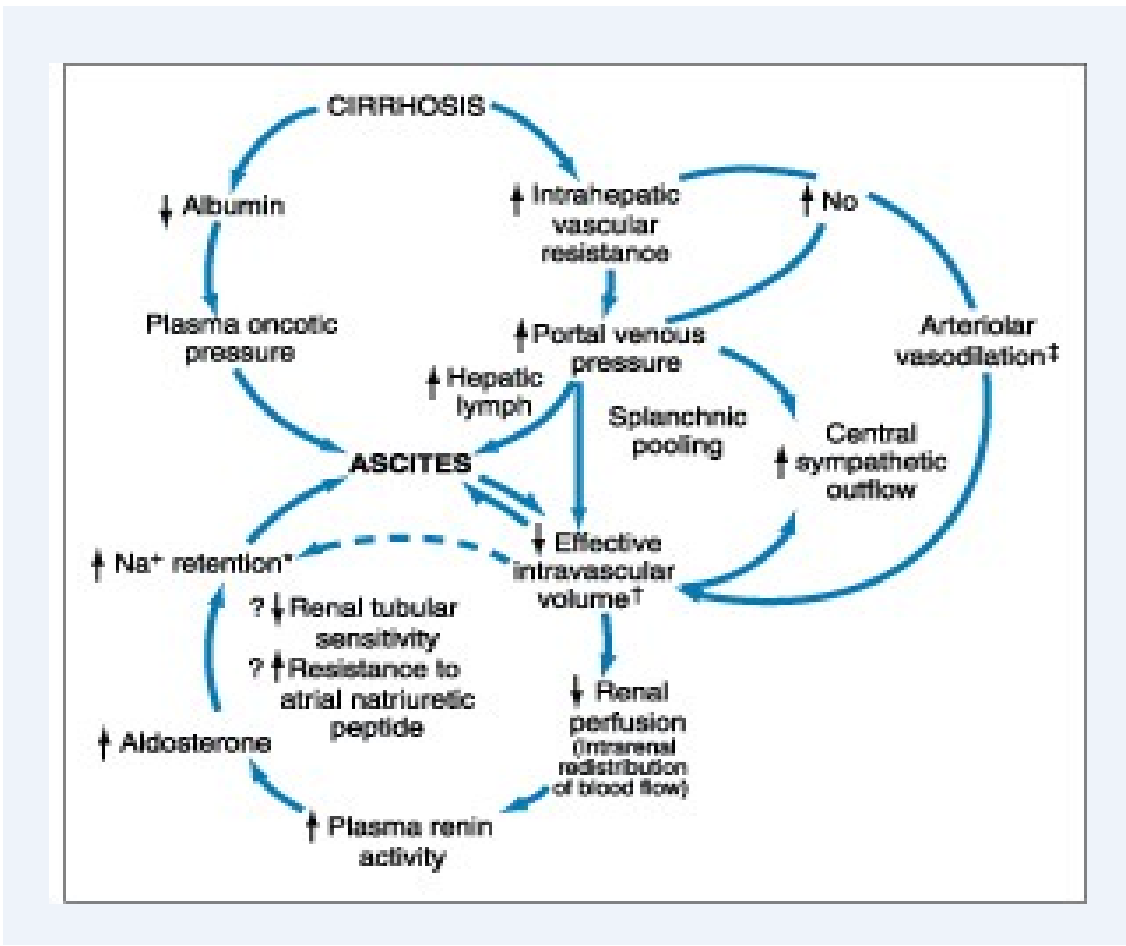
FLOW CHART (6)

SHOWS THEORIES OF ASCITES



FLOW CHART (7)

SHOWS RELATIONSHIP BETWEEN ASCITES VS PHT



ASCITES MORBIDITY/MORTALITY

- 3 year mortality rate of cirrhotic patients with episodic ascites shows 50% .
- But refractory ascites leads to poor prognosis having survival rate of 1 year rate of 50%[24] and less .
- Complications due to ascites are SBP, HRS[25,26], AND HE, HYPOPROTENEMIA.

Treatment of ascites

1) If the combination of spironolactone 100 mg/day or 10 mg/day of amiloride) and furosemide 40 mg/day orally is ineffective in increasing urinary sodium or decreasing body weight, the doses of both drugs should be increased simultaneously as needed (e.g.,spironolactone 200 mg plus furosemide 80 mg, then 300 mg plus 120 mg, and finally 400 mg plus 160 mg).
2) Severely sodium-restricted diets (e.g., 500 mg, or 22 mmol, sodium/day) are feasible
3) Antibiotics in SBP
4) Paracentesis
5) Albumin transfusion
6) Terlipressin in patients with hepato renal syndrome.

APPROACH OF REFRACTORY ASCITES

- International Ascites Club criteria defined refractory ascites which cannot be moblized instead of intensive medical therapy and persist even after one week of salt restricted diet or type1-diuretic resistant

- Type 2 is ascites which is diuretic intractable5 to 10% of patients with ascites develop refraction to treatment.[26]

- **Refractory Ascites**

Refractory ascites is defined as ascites unresponsive to a sodium-restricted diet and high-dose diuretic treatment.

Refractoriness may be manifested by minimal or no weight loss despite diuretics or the development of complications of diuretics.

FOLLOWING CRITERIAS ARE ESSENTISAL FOR

DIAGNOSING REFRACTORY ASCITES

DIAGNOSTIC CRITERIA

1. *Treatment duration*: Patients must be on intensive diuretic therapy (spironolactone 400 mg/day and furosemide 160 mg/day)* for at least 1 week and on a salt-restricted diet of less than 90 mmoles/day or 5.2 g of salt/day.
2. *Lack of response*: Mean weight loss of < 0.8 kg over 4 days and urinary sodium output less than the sodium intake.
3. *Early ascites recurrence*: Reappearance of grade 2 or 3 ascites† within 4 weeks of initial mobilization.

DIAGNOSTIC CRITERIA

4. *Diuretic-induced complications*:
   a. *Diuretic-induced hepatic encephalopathy*: development of encephalopathy in the absence of any other precipitating factor.
   b. *Diuretic-induced renal impairment*: increase of serum creatinine by $> 100\%$ to a value > 2 mg/dl in patients with ascites responding to treatment.
   c. *Diuretic-induced hyponatraemia*: decrease of serum sodium by > 10 mmol/L to a serum sodium of < 125 mmol/L.
   d. *Diuretic induced hypo or hyperkalaemia*: change in serum potassium to < 3 mmol/L or > 6 mmol/L despite appropriate measures.

SPONTANEOUS BACTERIAL PERITONITIS

- In 1975 conn coined the term SBP and exclude the surgical peritonitis cause of infection.[27]
- To diagnose spontaneous bacterial peritonitis
- Ascitic fluid should be culture positive and PML> 250 cells/mm 3 without surgical cause of abdominal infection[28].
- 25%of infections in ascites are SBP[29]
- Despite antibiotic treatment [30,31,32,33,34,35] In past 48% to 95% of patients died due to SBP.
- But in 1990”s because of early detection and antibiotic treatment mortality rate was reduced to 5%[35] with appropriate antibiotics.

PORTOSYSTEMIC OR HEPATIC ENCEPHALOPATHY

- Complications due to CLD either because of reduced liver cell function or increased portal hypertension.
- HE(36) defined as reversible cause of neurologic abnormality.
- Median survival is only 1 to 2% in pts with HE.

CLINICAL STAGES OF HE (TABLE-4)

Clinical Stage	Intellectual Function	Neuromuscular Function
Subclinical	Normal examination, but work or driving may be impaired	Subtle changes on psychometric or number connection tests
Stage 1	Impaired attention, irritability, depression, or personality change	Tremor, incoordination, apraxia
Stage 2	Drowsiness, behavioral changes, poor memory and computation, sleep disorders	Asterixis, slowed or slurred speech, ataxia
Stage 3	Confusion and disorientation, somnolence, amnesia	Hypoactive reflexes, nystagmus, clonus, and muscular rigidity
Stage 4	Stupor and coma	Dilated pupils and decerebrate posturing; oculocephalic reflex; absence of response to stimuli in advanced stages

PATHOGENESIS OF PORTO SYSTEMIC ENCEPHALOPATHY. THIS BELOW MECHANISM SHOWS MERCAPTANS AND AMMONIA PLAYING IMPORTANT ROLE IN HE [37]

(TABLE-5)

Mechanism	Hypothesis
Toxins (ammonia, mercaptans)	Ammonia and mercaptans produced by the action of intestinal bacteria on urea and protein are elevated in blood and brain as a result of defective hepatic clearance and lead to impaired neural function through cytotoxicity, cell swelling, and depletion of glutamate
GABAergic neurotransmission	Defective hepatic clearance of GABA produced by intestinal bacteria, increased neuronal GABA synthesis, and increased production of benzodiazepine receptor agonists leads to neuronal inhibition through stimulation of the GABA receptor complex in postsynaptic membranes
False neurotransmitters	Increases in the ratio of plasma aromatic amino acids to branched-chain amino acids increase brain levels of aromatic amino acid precursors of false neurotransmitters

* GABA, -aminobutyric acid.

BELOW TABLE SHOWS TREATMENT FOR HE(TABLE-6)

1. Identify and correct the precipitating cause(s)
a. Assess volume status, vital signs
b. Evaluate for gastrointestinal bleeding
c. Eliminate sedatives, tranquilizers, or similar drugs
d. Perform screening tests for hypoxia, hypoglycemia, anemia, hypokalemia, and other potential metabolic or endocrine factors and correct as indicated
2. Initiate ammonia-lowering therapy
a. Nasogastric lavage, lactulose ± other cathartics or enemas to remove the source of ammonia from the colon
b. Minimize or eliminate dietary protein
c. Initiate treatment with lactulose or lactitol to produce 2 to 4 bowel movements per day
d. Consider oral nonabsorbable antibiotics to reduce intestinal bacterial counts
e. Consider flumazenil and other benzodiazepine receptor antagonists (see text)
3. Minimize the potential complications of cirrhosis and depressed consciousness
a. Provide supportive care with attention to airway, hemodynamic, and metabolic status

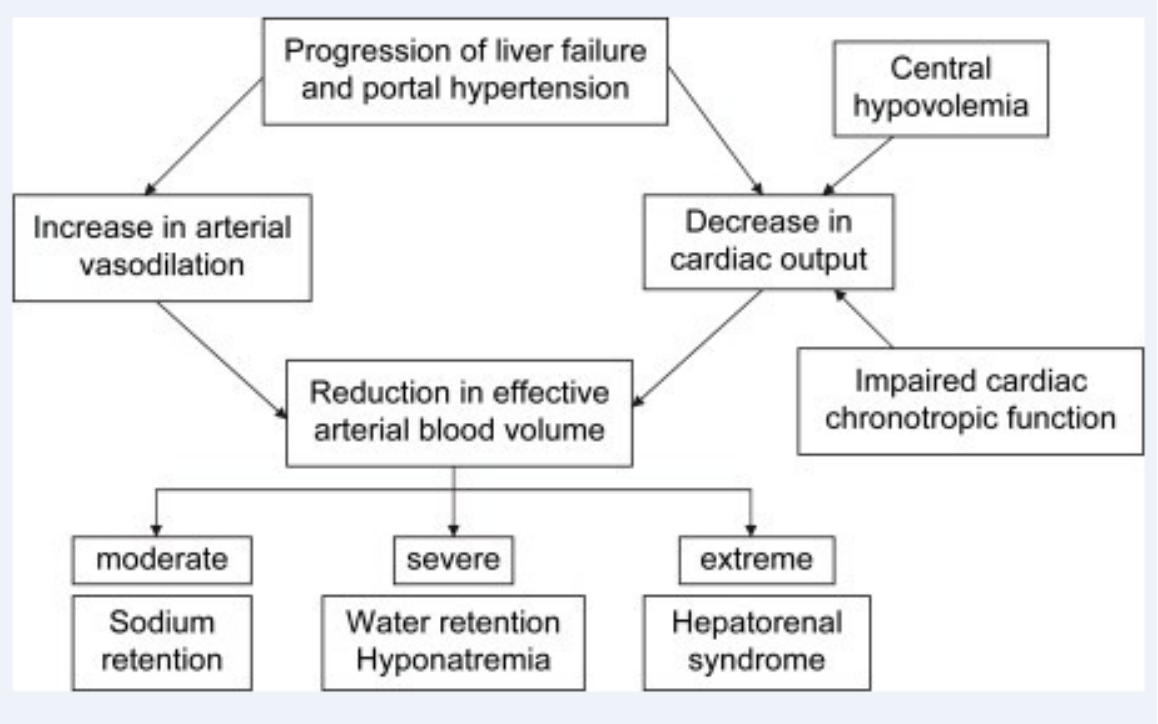
DEFINITION AND PATHOPHYSIOLOGY OF HRS

- HRS defined as funtional renal failure without structural abnormality or intrinsic renal disease.[38,39]
- The peculiar features of HRS is intrinsic reno vascular constriction at cortex which leads to sodium retension[40,41,42] and oliguria
- In cirrhotics HRS incidence is around 15%.
- Median survival in people with liver disease developing hepato renal syndrome is around 6 months [43] only which directly implicate the one of the paramount cause of high mortality.

(TABLE-7) SHOWS TYPES OF HRS

Hepatorenal Syndrome Type 1	Hepatorenal Syndrome Type 2
• Rapid rise in the serum creatinine level • Doubling of the initial serum creatinine level greater than 2.5mg/dl in less than 2 weeks • Prognosis: poor; usually occurs secondary to precipitating factors including SBP, gastrointestinal bleeding, large voume paracentesis • Inpatient-ICU • Treatment: Terlipressin, Norepinephrine, Midodrine, Ocreotide • Transplant • Prognosis: 10 percent survival at 90 days	• Gradual increase in the serum creatinine level • Slow rise above 1.5 mg/dl • Associated with diuretic resistant refractory ascites • Outpatient close follow up • Treatment: Midodrine, Ocretotide • Transplant • Prognosis: 6 months without treatment

MECHANISM OF PHT CAUING HRS FLOW CHART - 8



FACTORS PREDICTING PHT AND VARICEAL BLEEDING:

Local Factors			
Variceal size, vessel radius			
Variceal wall thickness, red signs			
Hemodynamic Factors			
Portal (intravariceal) pressure: threshold HVPG of 12 mm Hg			
Blood volume			
Collateral blood flow (?)			
Intra-abdominal pressure (?)			
Severity of Liver Disease (Child-Turcotte-Pugh Class)			
	Numerical score		
Parameter	1	2	3
Ascites	None	Slight	Moderate/severe
Encephalopathy	None	Slight/moderate	Moderate/severe
Bilirubin (mg/dL)	<2.0	23	>3.0
Albumin (mg/L)	>3.5	2.83.5	<2.8

VARICEAL BLEEDING CAUSES

Determining factors of bleeding from varices Are

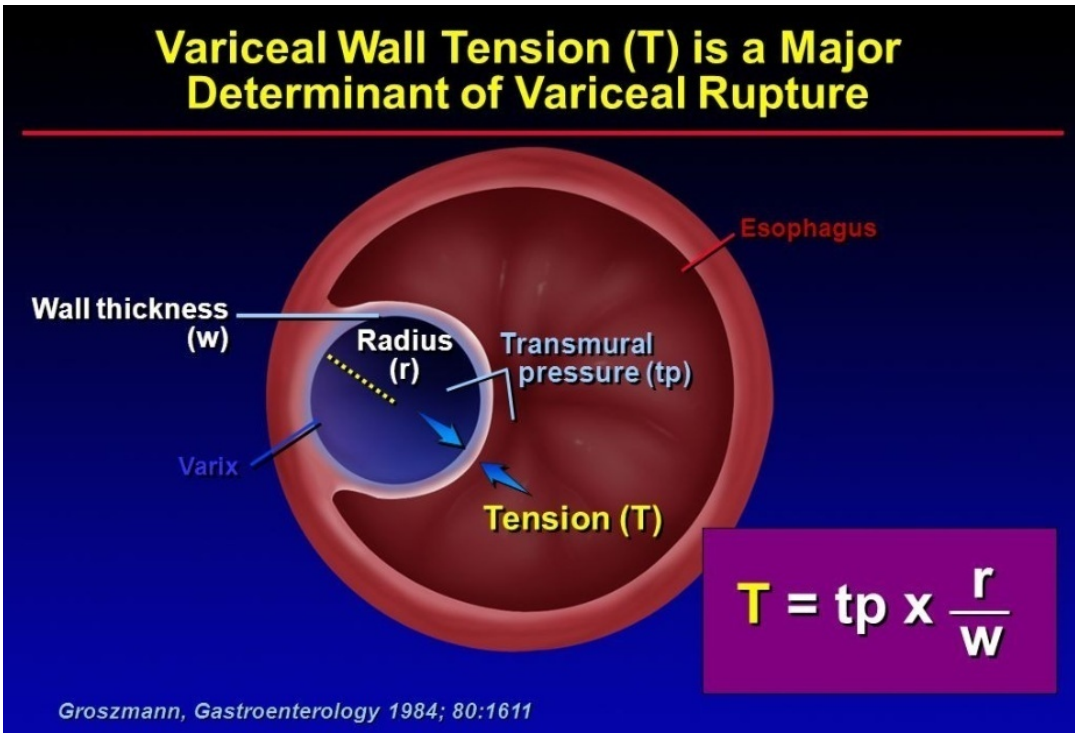
1) Variceal size, wall thickness, transmural pressure[44]

2) HVPG >12mm hg

3) Red color signs(red weal marks seen by endoscopy)[44]

4) Liver failure severity measured by CTP score

FIGURE- 9 SHOWS MEASUREMENT OF VARICEAL PRESSURE



- Explosion theory which explains explosive rupture of [45,46 ,47] varices occurs if elastic wall tension increases to a critical level

  AASLD,EASL,APASL : classifies for practical approach as

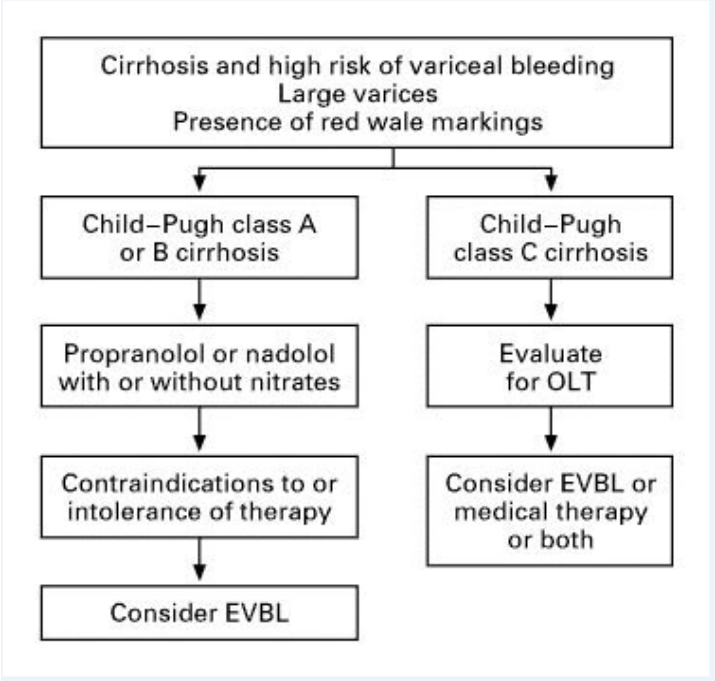
  1) Small and large varices

  2) With red color signs presence or absence .

PROGNOSIS OF VARICEAL HAEMORRHAGE

- ONE OF THE DEADLY COMPLICATION from PHT is variceal bleeding which leads to one third of death in patients with cirrhosis.[48,49,50,51]

APPROACH FOR MANAGEMENT OF BLEEDING VARICES(FLOW CHART-9)



PATIENTS WITH CIRRHOSIS DEVELOPING DISEASE

DIVIDED IN TO FIVE STAGES(FLOW CHART-10)

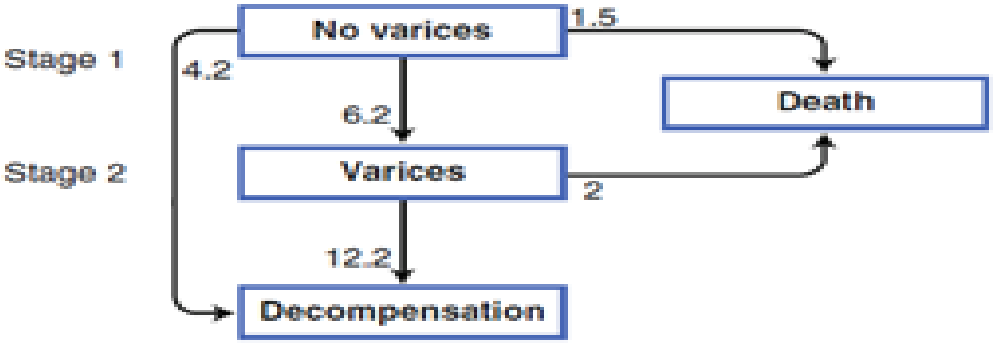
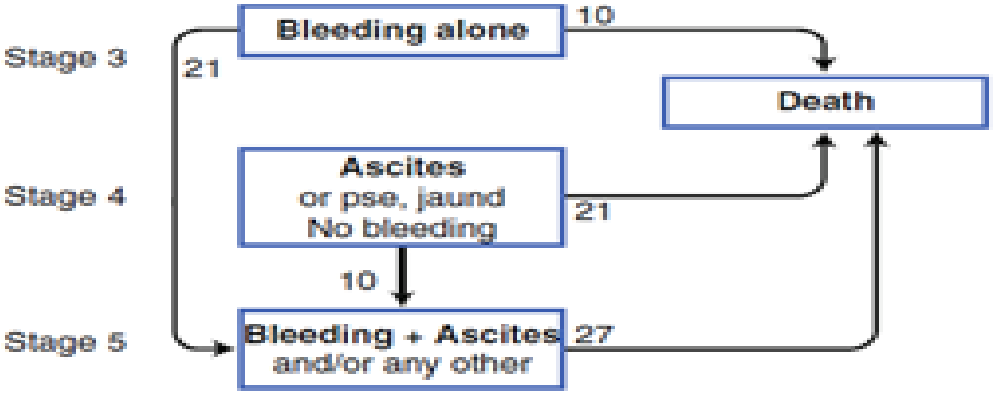


FIG 2



ASSESSMENT OF PROGNOSIS IN LIVER DISEASE

- Well studied and valuble prognostic indicators are
- CTP score-child turcott pugh score used to predict short term mortality but not useful to assess long term outcome.
- This score depends albumin, bilirubin, ascites, encphelopathy, jaundice, and coagulopathy i.e: PT/INR [52]

(TABLE –8) DESCRIBES CTP SCORE

Child-Turcotte-Pugh Classification for Severity of Cirrhosis			
Clinical and Lab Criterias	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time Seconds prolonged International normalized ratio	 <4 <1.7	 4-6 1.7-2.3	 >6 >2.3
***Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)** Class A = 5 to 6 points (least severe liver disease) Class B = 7 to 9 points (moderately severe liver disease) Class C = 10 to 15 points (most severe liver disease)			

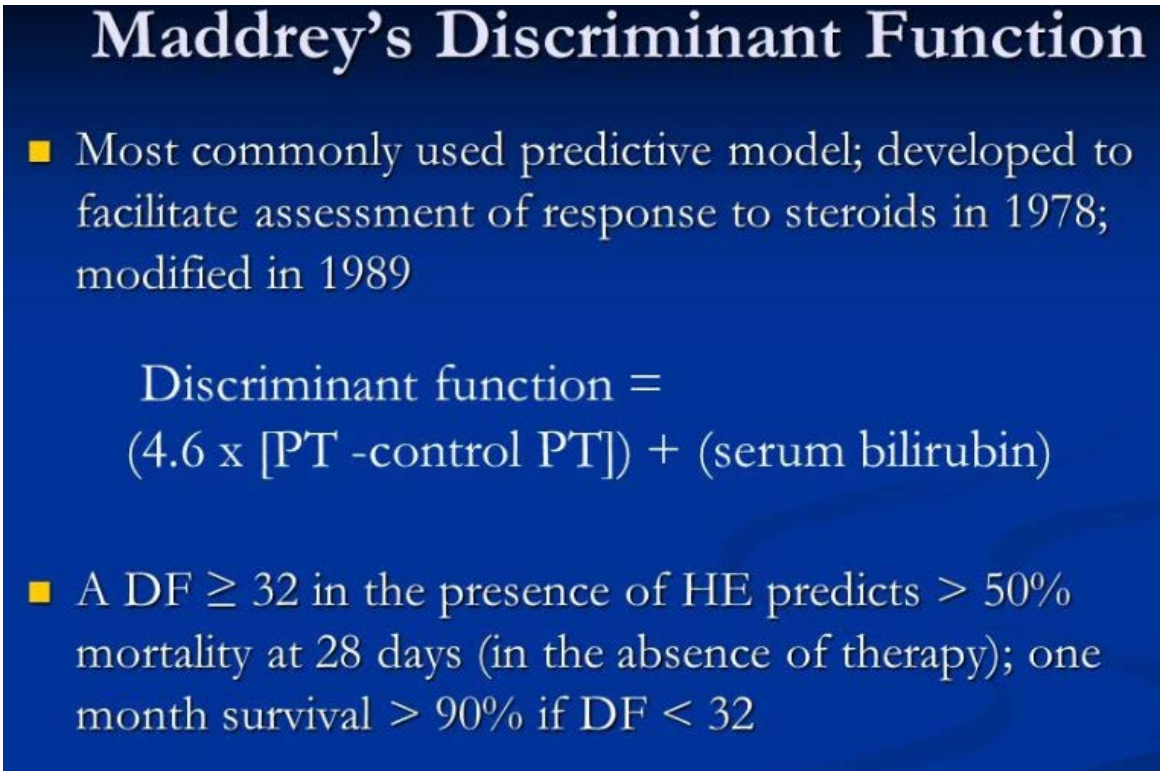
- A well designed mathematical model is MELD SCORE which helps to determine prognosis in patients selected for TIPS .
- It helps to predict mortality in patients waitlist for transplantation.[53]
- This score depends serum creatinine, bilirubin, Prothrombin time.

Now addition Na in MELD improves the accuracy to predict the outcome of disease.[54]

MELD SCORE

- MELD = 3.8(SERUM BILIRUBIN –MG/DL)+11.2 IN INR + 9.6 IN SERUM CREATININE – MG/DL+ 6.4

MDF[55]- HELPS TO PREDICT MORTALITY IN ALCOHOLIC HEPATITIS PATIENT.



- HVPG another indepentent predictor to assess the death
- An acute phase reactant serum ferritin shows a very good prognostic indepent marker to predict mortality in decompensated liver disease and also like MELD score used to assess mortality in cirrhotics who awaited for transplantation.
- Another peculiar thing is serum ferritin used in alcoholics as well as NAFLD patients.[56,57,58]

- Hyperferritinemia associated with hepatic iron overload and leads to liver injury and fibrosis[59].this mechanism of iron induced cell injury known as ferroptosis.[60]

MATERIALS AND METHODS

STUDY DESIGN

- This is a prospective analytical study of 100 cases of patients with liver disease in decompensated stage admitted in government Mohan Kumaramangalam medical college tertiary care hospital, in salem evaluated during the period of JUNE 2016 to JUNE 2017.
- After getting informed consent patients enrolled in our study.
- After approval by our institute ethical committee data retrived from medical records.

INCLUSION CRITERIA

- Age group above 35 yrs and above with CLD
- Patients with chronic liver disease diagnosed under AASLD guidelines
- Patients with radiological proven contracted liver ,
- with endoscopy findings of oesophageal varices
- With portal vein measurements of >13 mm
- According to APASL guidelines patients with acute on chronic liver cell failure

(TABLE-9)

Asia pacific Association of study of liver diseases (APASL) consensus guidelines
Acute hepatic insult manifesting as jaundice (serum Bilurubin = 5 mg/dL)and coagulopathy(INR = 1.5 or prothrombin activity <40%), complicated within 4 weeks by ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease.
Working definition by EASL-AASLD on ACLF
Acute deterioration of pre-existing, chronic liver disease, usually related to a precipitating event and associated with increased mortality at 3 months due to multi-system organ failure

EXCLUSION CRITERIA

1) Age bellow 35 yrs

2) Womans with pregnancy

3) Patients with hepatocellular carcinoma

4) Patients with chronic disease like tuberculosis

5) PLWHA patients

6) Patients on hepatotoxic drugs.

COLLECTIONS OF DATA METHOD

- After arriving the provisional diagnosis of chronic liver disease demographic data retrieved which includes Age, Sex, Co-morbidity, medical history, any native medications and drugs.
- Information gathered from patient and attenders in the case of liver disease with hepatic encephalopathy and entered in the proforma designed for this study.
- Using AUDIT-C questionnaires alcohol intake identified.
- Medical history obtained regarding jaundice, altered sleep pattern, ascites, haematemesis, oliguria.
- After thorough head to foot examination findings included in the proforma which have information like icterus, spider naevi, gynecomastia, pedal edema, hepatomegaly, spleenomegaly, abdominal wall collaterals, testicular atrophy in males.
- Patients without encephalopathy and conscious status thorough neurological assesment done with mini mental status. By using west heaven criteria in the presence of encephalopathy classified the patients and entered in the records.

- Lab investigations included complete haemogram, PT/INR, LFT, RFT, serum electrolytes, serum ferritin by using Roche electrochemiluminance assay, VCTC, viral markers including HBV and anti HCV.
- According to international ascites club(61) and AASLD guidelines[62] ascites, SBP and HRS are classified respectively.
- Imaging done by USG abdomen to all patients.CT and MRI done if needed patients.
- Upper GI endoscopy done to all the studied population and we graded the varices with paquet classification.

(TABLE-10)

Grade 0	Absence of esophageal varices
Grade I	Microcapillars located on esophagogastric transition or distal esophagus
Grade II	1 or 2 small varices located on distal esophagus
Grade III	Medium varices
Grade IV	Large varices in any part of the esophagus

– Endoscopic classification of esophageal varices according to Paquet[11]

DISEASE SEVERITY ASSESMENT

- In alcoholic hepatitis by using maddreys discrimination score was used.
- To assess the severity of the disease and to prognosticate the patient MELD score was applied.
- By using dichomatous variable which is categorical variables serum ferritin levels divided whether its normal or elevated .
- Enrolled patients were followed for 1year and mortality was assesed at 15^{th} and 30^{th} day of evaluation.

ANALYSIS BY STATISTICS METHODS

To describe about data descriptive statistics frequency analysis,used. Percentage analysis were used for categorical analysis. For continuos variables the Mean and SD were used.

To find the significant difference between the bivariate samples in independent groups the un paired sample t-test was used.

By using correlation analytical method we assess how much significant to predict mortality in decompensated liver disease with serum ferritin.

Statistical methods by applying correlation guide us how this two variables either categorical or numerical measurements are related.

The strength of association between two variables assed by bivariant analysis known as Pearson”s correlation co efficient (r).

We have to correlate two variables in single person for that by using chi-squared test which is conclude whether association between two variables are significant or not.chi squared and Fishers exact was used to found categorical data significance.

Ripper algorithm applied to separate the serum ferritin values and we found SF< 298 associated with low mortality and SF>298 with high mortality in our studied 100 patients with liver disease.

Expansion of RIPPER is Repeated incremental pruning to produce Error Reduction. By applying this propositional rule learner we found serum ferritin studied in our population if more than 298 having high mortality.

Microsoft XL sheet was used to tabulate the datas and SPSS software23 version was used for statistical analysis.

IN all the above statistical tools P value (probability)0 .05 was considered as significant level. P<_.01 was taken as highly significant.

P value >.05 was nil significant.

RESULTS AND OBSERVATIONS (TABLE-11) :

Attributes taken for study

S.No	Name of the Attributes
1.	AGE
2.	SEX
3.	MELD SCORE
4.	ASCITIES
5.	URINE OUT PUT
6.	ALTERED SENSORIUM
7.	LFT
8.	HB % (gms)
9.	PLATELETS (L/CU MM)
10.	T.PROTIEN
11.	ALBUMIN
12.	T.BILIRUBIN
13.	D.BILIRUBIN
14.	SGOT
15.	SGPT
16.	s.ALP
17.	HBS AG
18.	ANTI HCV
19.	BT
20.	CT
21.	PT/INr
22.	B.UREa
23.	S.CREATININE
24.	OESOPHAGEAL VARICES
25.	POLYMORPHS

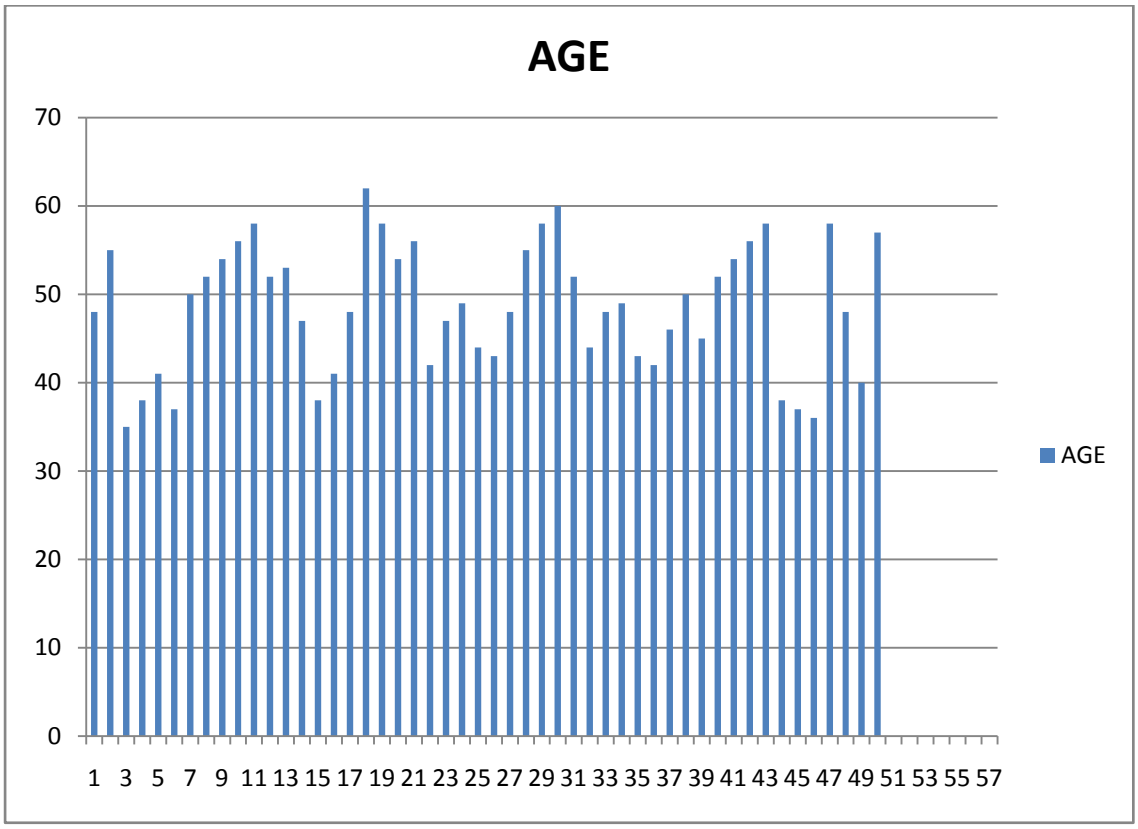
Table 12: Maximum and Minimum values of numerical Attributes taken for study

S.No	Name of the Attributes	Minimum	Maximum
1.	AGE	35	62
2.	MELD SCORE	15	45
3.	HB % (gms)	9.6	12
4.	PLATELETS (L/CU	0.8	3.2
5.	T.PROTIEN	2.4	8.1
6.	ALBUMIN	3.4	4.9
7.	T.BILIRUBIN	1.9	32.6
8.	SGOT	4	211
9.	SGPT	6	162
10.	s.ALP	13	320
11.	BT	2	9.2
12.	CT	8	18.5
13.	PT/INr	1	4.1
14.	B.UREa	18	234
15.	S.CREATININE	0.6	16.2
16.	OESOPHAGEAL	31(n0)	69(yes)
17.	POLYMORPHS	14(no)	86(yes)
18.	Maddray Index	<32	>32

Every attribute in the dataset is compared with its corresponding SF values and its correlation is measured using Chi Squared and Pearson correlation analysis.

1.ACCORDING TO AGE DISTRIBUTION: DEMOGRAPHIC DATA

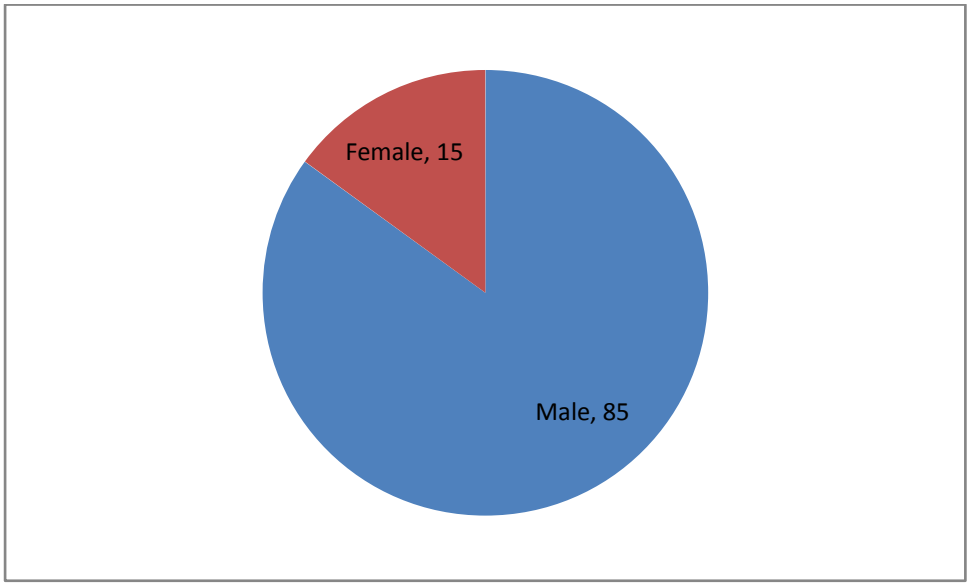
BELOW GRAPH (CHART-11) A shows age distribution among 100 patients minimum age was 35 and maximum one was 62 yrs.



2.ACCORDING WITH GENDER PATIENT DISTRIBUTION DATA (PIECHART-12) SHOWING THE GENDER DISTRIBUTION IN THE STUDIED POPULATION.

15% ARE FEMALES

85% ARE MALES.

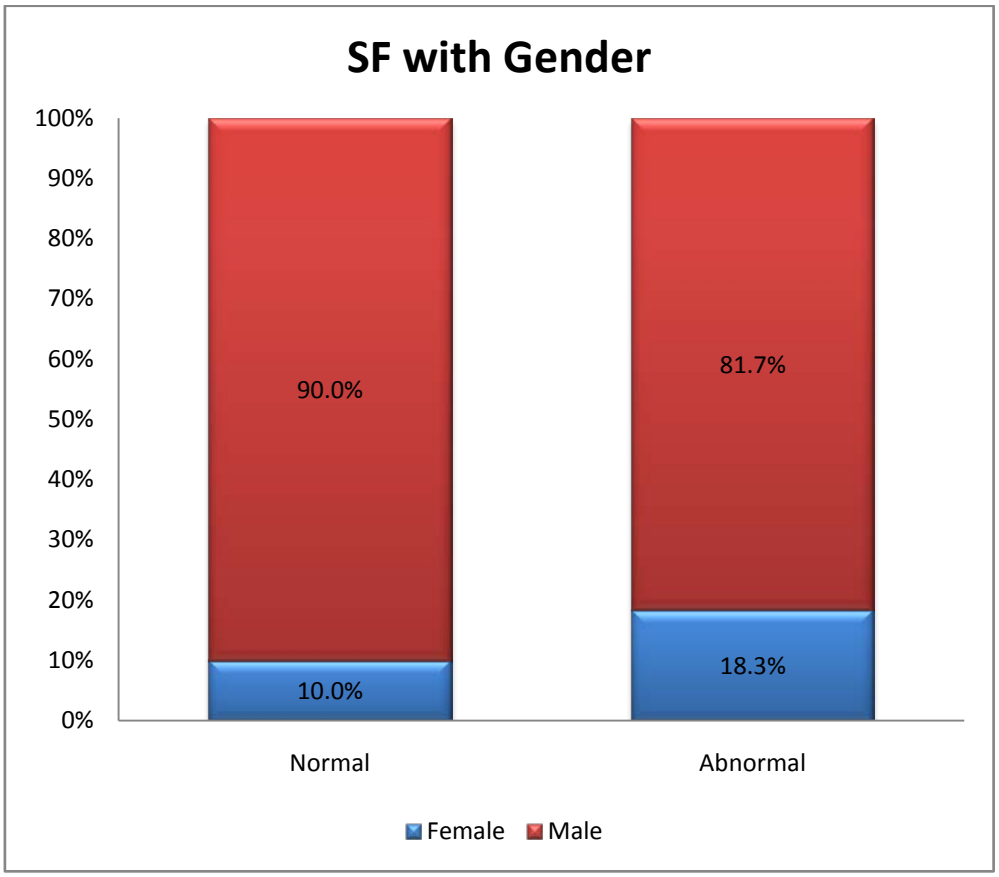


graph b shows correlation between sf and gender .

18.3% of females and 81.7% of males shows elevated serum ferritin.in our study group maximum number of enrolled patients are males.

since in india alcoholism and liver disease higher in males than females we are not able to come to conclusion whether sf level associated with gender specificity.

(BAR CHART-13). SHOWING CORRELATION BETWEEN SF WITH GENDER.



FIRST ATTRIBUTE GENDER IS CORRELATED WITH SF VALUES AND ARE SHOWN IN TABLE 13 AND 14.

COMPARISON OF SF WITH GENDER IS GIVEN IN TABLE 13

CROSSTAB

			SF		
			Normal	Abnormal	Total
SEX	F	Count	4	11	15
		% within SF	10.0%	18.3%	15.0%
	M	Count	36	49	85
		% within SF	90.0%	81.7%	85.0%
Total		Count	40	60	100
		% within SF	100.0%	100.0%	100.0%

TABLE 13 COMPARISON OF SF WITH SEX

CORRELATION ANALYSIS OF THE ATTRIBUTES SF WITH SEX IS SHOWN IN TABLE 14

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.307[a]	1	.253		
Continuity Correction[b]	.735	1	.391		
Likelihood Ratio	1.366	1	.243		
Fisher's Exact Test				.392	.197
N of Valid Cases	100				

Table 14 Correlation analysis between attributes **SF with sex**

From table 13 and 14 its inferred that there is no significant correlation between SF with gender values of the patient taken for study.

3.Next attribute Ascities is compared with attribute SF values and shown below.

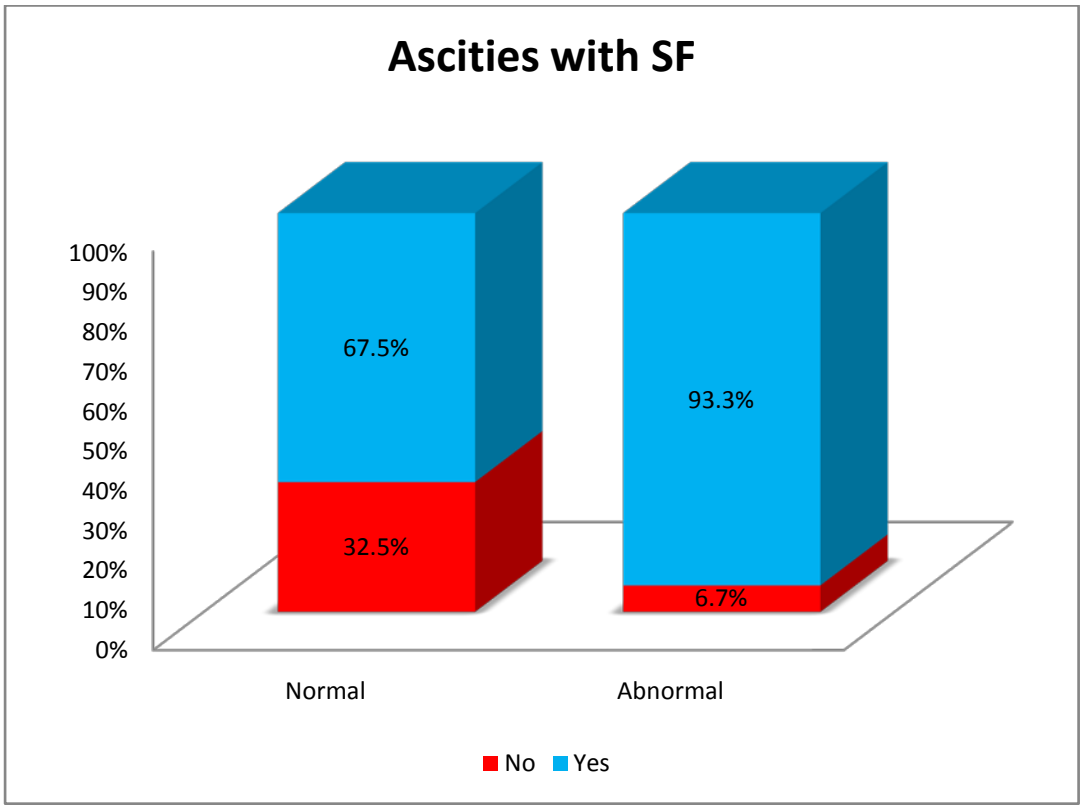


CHART 14 Comparison of Ascities values with SF values

The correlation analysis between these two attributes are shown in Table 15

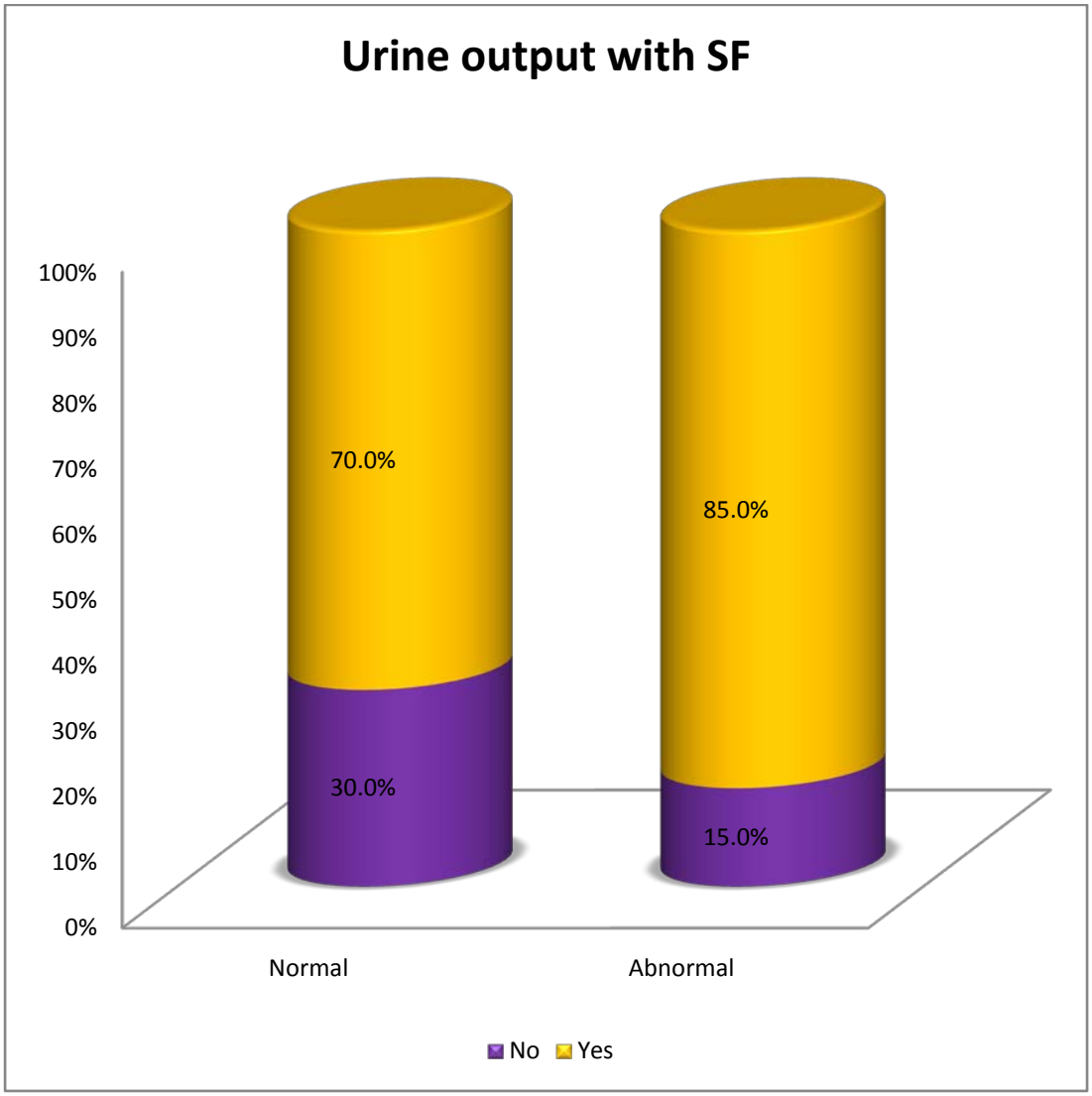
CHI-SQUARE TESTS

	Value	**df**	**Asymp. Sig. (2-sided)**	**Exact Sig. (2-sided)**	**Exact Sig. (1-sided)**
Pearson Chi-Square	11.351[a]	1	.001		
Continuity Correction[b]	9.594	1	.002		
Likelihood Ratio	11.339	1	.001		
Fisher's Exact Test				.001	.001
N of Valid Cases	100				

Table 15 Correlation analysis of Ascities values with SF values

From table 15, we incur that P- value of the comparison is less than or equal to 0.01. This indicates that there is high correlation between, Ascites values with SF values. This also proves that high SF values are tightly associated with Asities which may lead to high mortality.

4.The next attribute to be compared with SF attribute is Urine output and is shown in Graph 15



Graph 15 Comparisons of **Urine output with SF**

THE CORRELATION ANALYSIS BETWEEN THESE TWO ATTRIBUTES ARE SHOWN IN TABLE 16

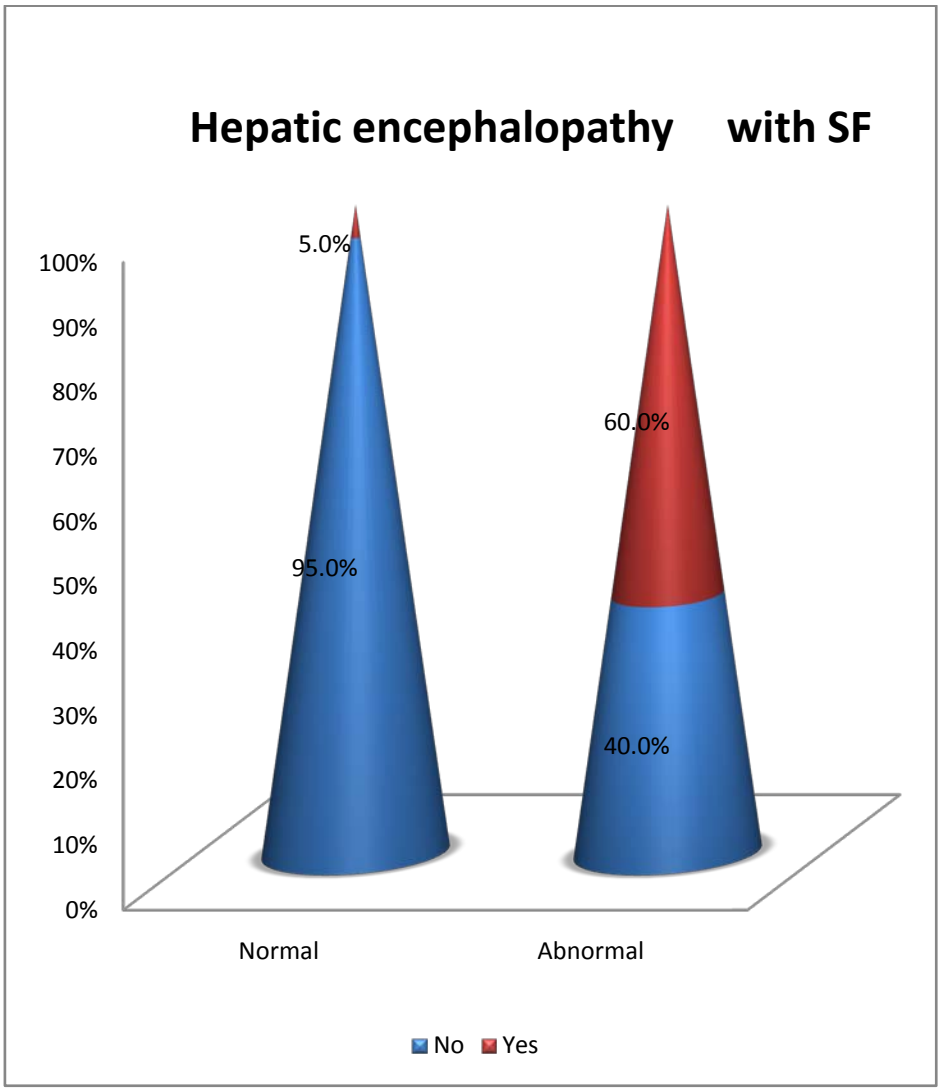
Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.255[a]	1	.071		
Continuity Correction[b]	2.414	1	.120		
Likelihood Ratio	3.197	1	.074		
Fisher's Exact Test				.084	.061
N of Valid Cases	100				

Table 16 Correlation analysis of **Urine output with SF**

From table 16 we incur that P- value of the comparison is less than 0.05. This indicates that there is no significant correlation between, urine output values with SF values. This also proves that high SF values are not highly associated with urine output values which needs further analysis to be performed.

5.The next attribute to be compared with SF attribute is Hepatic encephalopathy and is shown in (CHART : 16).



Graph 1.3 Comparisons of Hepatic encephalopathy **with SF**

THE CORRELATION ANALYSIS BETWEEN THESE TWO ATTRIBUTES ARE SHOWN IN TABLE 17.

Chi-Square Tests

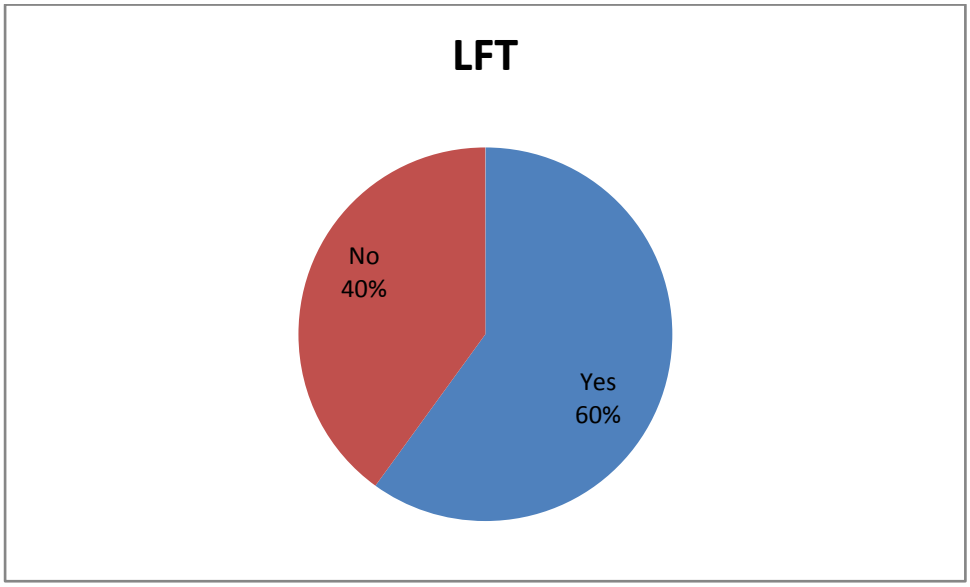
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	30.815[a]	1	.000		
Continuity Correction[b]	28.525	1	.000		
Likelihood Ratio	36.170	1	.000		
Fisher's Exact Test				.000	.000
N of Valid Cases	100				

Table 17. Correlation analysis of Hepatic encephalopathy **with SF**

From table 17. we incur that P- value of the comparison highly significant . This indicates that there is high correlation between, Hepatic encephalopathy values with SF values. This also proves that high SF values are highly associated with Hepatic encephalopathy values which leads to high mortality.

6.The next attribute to be compared with SF attribute is LFT and is shown in

(PIE CHART- 17) SHOWING DISTRIBUTION OF ELEVATED LFT AMONG STUDIED POPULATION.



PIE CHART :17

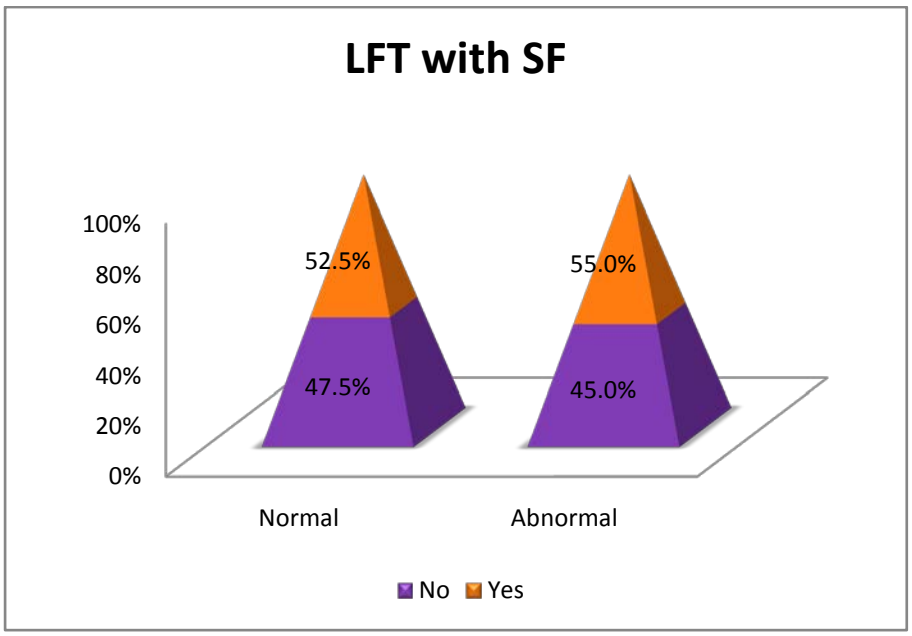


CHART 18: Comparisons of LFT **with SF**

THE CORRELATION ANALYSIS BETWEEN THESE TWO ATTRIBUTES ARE SHOWN IN TABLE 18

Chi-Square Tests

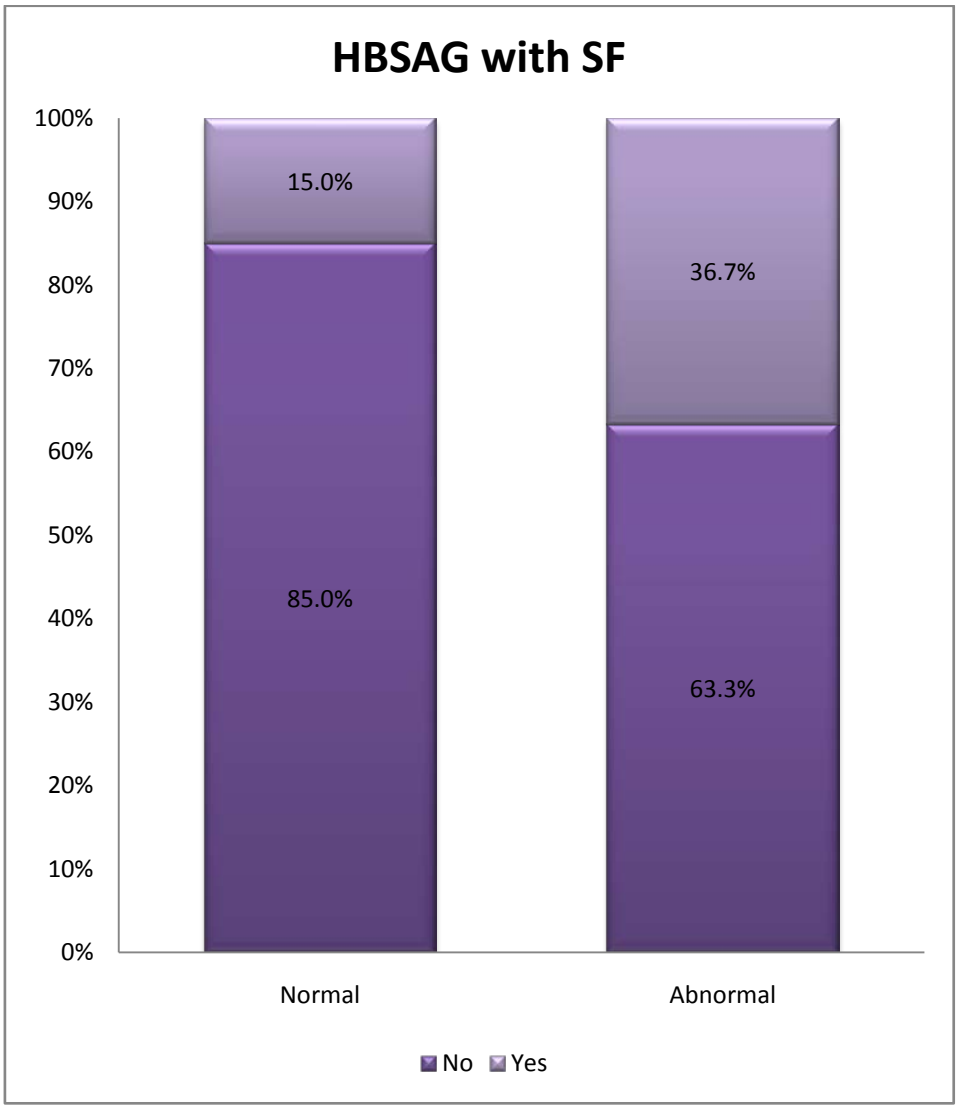
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.060[a]	1	.806		
Continuity Correction[b]	.002	1	.967		
Likelihood Ratio	.060	1	.806		
Fisher's Exact Test				.840	.483
N of Valid Cases	100				

Table 18 Correlation analysis of LFT w**ith SF values**

From table 18 we incur that P- value of the comparison non significant . This indicates that there islow correlation between, LFT values with SF values. This also proves that high SF values are having low association with LFT values which NEEDS more investigation.

7. The next attribute to be compared with SF attribute is HBS AG and SF is shown in

CHART 19



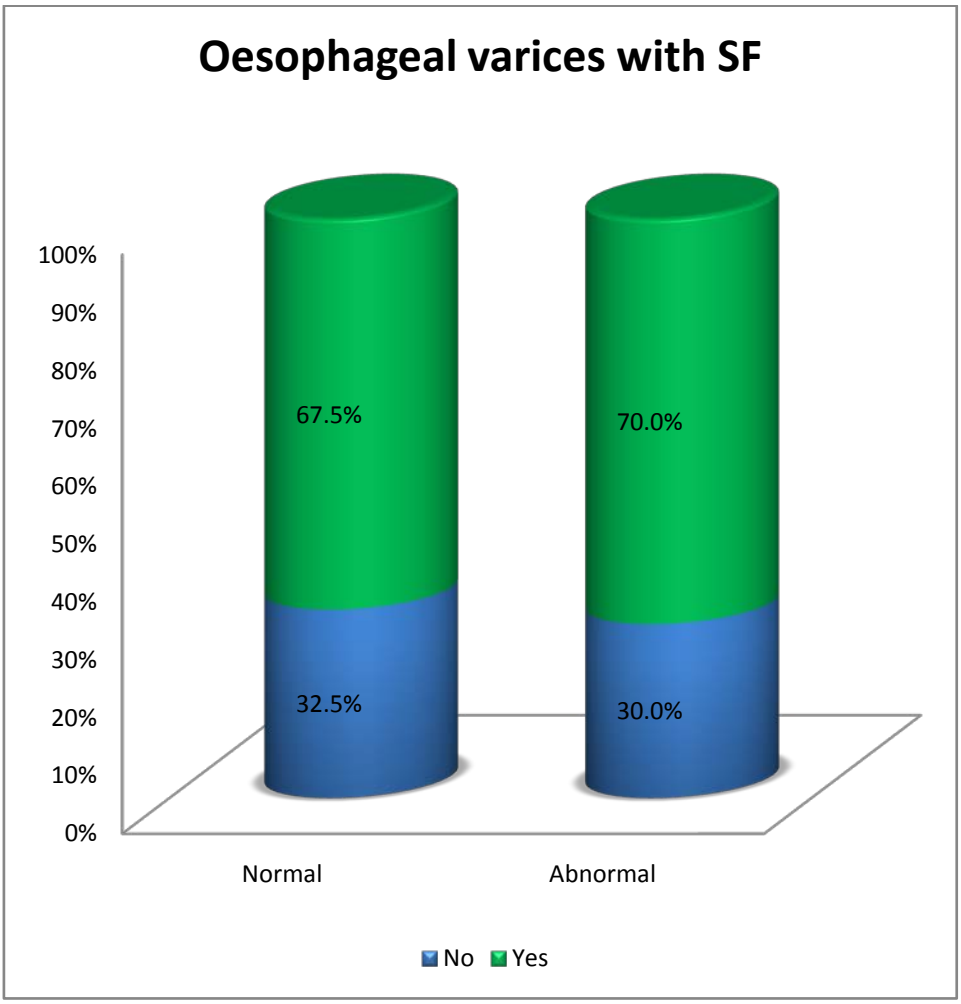
Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	5.589[a]	1	.018		
Continuity Correction[b]	4.566	1	.033		
Likelihood Ratio	5.915	1	.015		
Fisher's Exact Test				.023	.015
N of Valid Cases	100				

TABLE 19 CORRELATION ANALYSIS OF HBSAG POSITIVE PATIENTS W**ITH SF VALUES**

From table 19 we incur that P- value of the comparison highly significant . This indicates that there is high correlation between, Hepatitis B antigen positivity values with SF values. Since the patients presented with decompensated liver status and found HBSAG positivity incidently by routine investigations elevated serum ferritin level may be due to further aggravated by viral induced liver damage.so we need to study separately in future whether serum ferritin will help to indentify as a prognostic indicator in HBSAG positive patients with dcld.

8.THE NEXT ATTRIBUTE TO BE COMPARED WITH SF ATTRIBUTE IS OESOPHAGEAL VARICES AND SF IS SHOWN IN (CHART - 20)



Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.070[a]	1	.791		
Continuity Correction[b]	.002	1	.965		
Likelihood Ratio	.070	1	.791		
Fisher's Exact Test				.828	.480
N of Valid Cases	100				

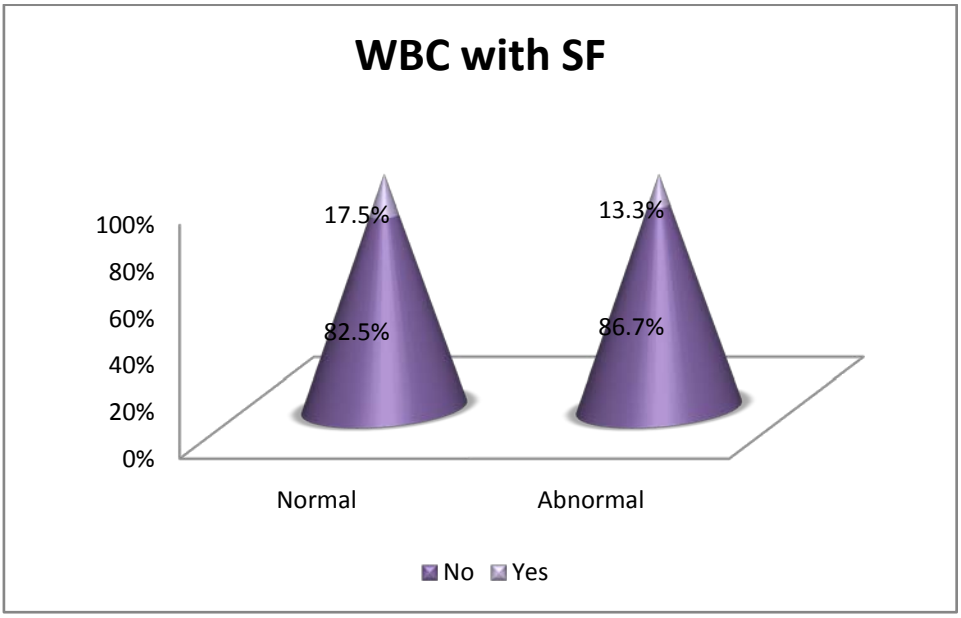
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 12.40.

b. Computed only for a 2x2 table

TABLE 20 CORRELATION ANALYSIS OF OESOPHAGEAL VARICES WITH SF VALUES

From table 20 we incur that P- value of the comparison non significant . This indicates that there is low correlation between, oesophageal varices with SF values. Since each patient may or maynot develop varices and variceal grades are also vary between patients.so we have to study elaborately in future about variceal grades and associated value of serum ferritin.

9.THE NEXT ATTRIBUTE TO BE COMPARED WITH SF ATTRIBUTE IS WBC COUNT AND SF IS SHOWN IN CHART- 21



Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.327[a]	1	.568		
Continuity Correction[b]	.082	1	.775		
Likelihood Ratio	.323	1	.570		
Fisher's Exact Test				.580	.383
N of Valid Cases	100				

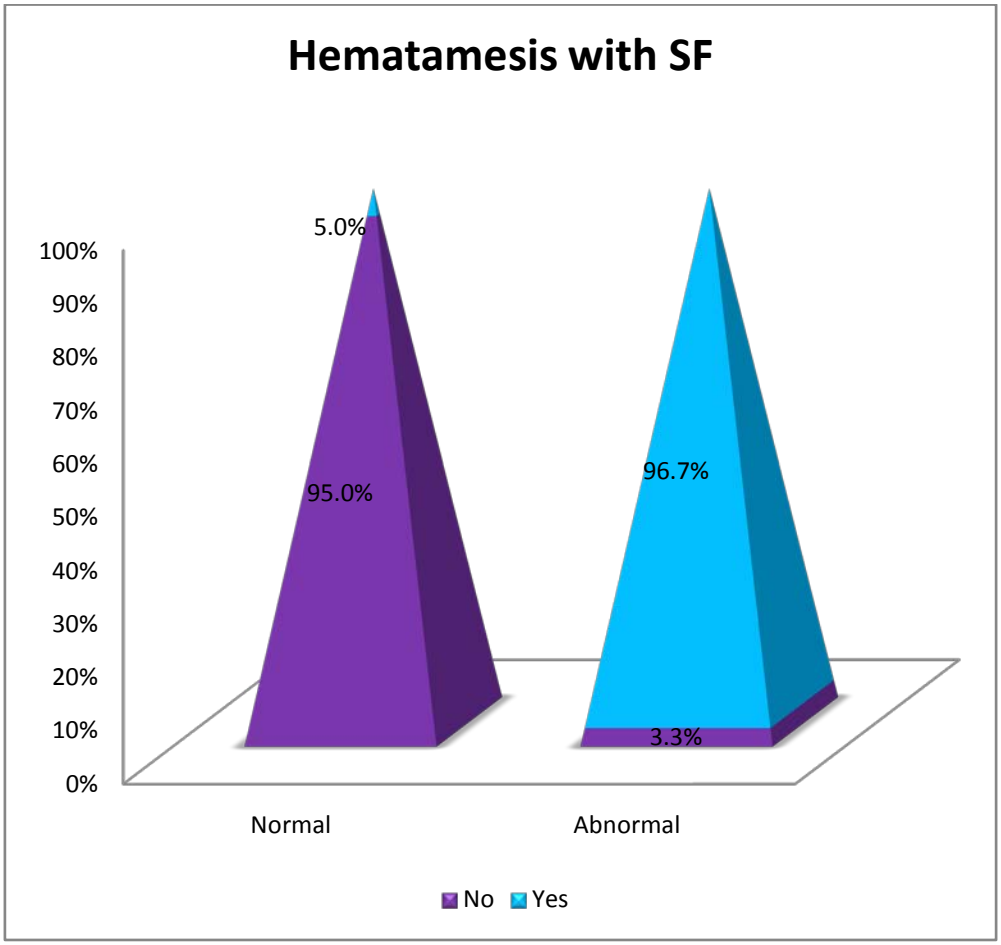
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 6.00.
b. Computed only for a 2x2 table

TABLE 21 CORRELATION ANALYSIS OF WBC WITH SF VALUES

From table 21 we incur that P- value of the comparison non significant . This indicates that there is low correlation between, WBC values with SF values.because of varied white blood cell count we are not able to corrulate.some of the patients have high count due to spontaneous bacterial peritonitis ,some of the patients have low count due to hypersplenism or alcohol induced bone marrow suppression.

10.THE NEXT ATTRIBUTE TO BE COMPARED WITH SF ATTRIBUTE IS HEMATAMESIS AND SF IS SHOWN IN

(CHART-22)



Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	84.028[a]	1	.000		
Continuity Correction[b]	80.252	1	.000		
Likelihood Ratio	101.184	1	.000		
Fisher's Exact Test				.000	.000
N of Valid Cases	100				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 16.00.

b. Computed only for a 2x2 table

TABLE 22 CORRELATION ANALYSIS OF HEMATEMESIS WITH SF VALUES

From table 22 we incur that P- value of the comparison highly significant. AND INDICATES DEFINITE CORRULATION OF HIGH SERUM FERRITIN LEVEL WITH HEMATEMESIS.IN DCLD MOST OF THE PATIENTS DIED BECAUSE OF HEMATEMESIS WHICH IS SIGNIFICANTLY CORRELATED WITH HIGH FERRITIN VALUES.

11.COMPARISON OF MELD SCORE VALUE AND MORTALITY RATE

MELD score calculated in all the 100 patientstaken for study.and found that score >25 landed up with high mortality.

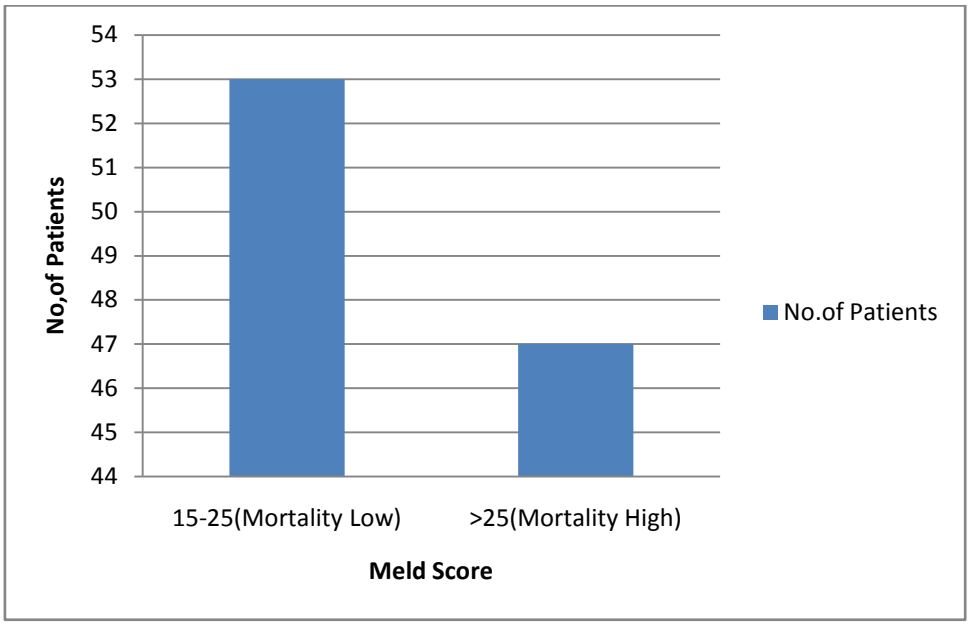
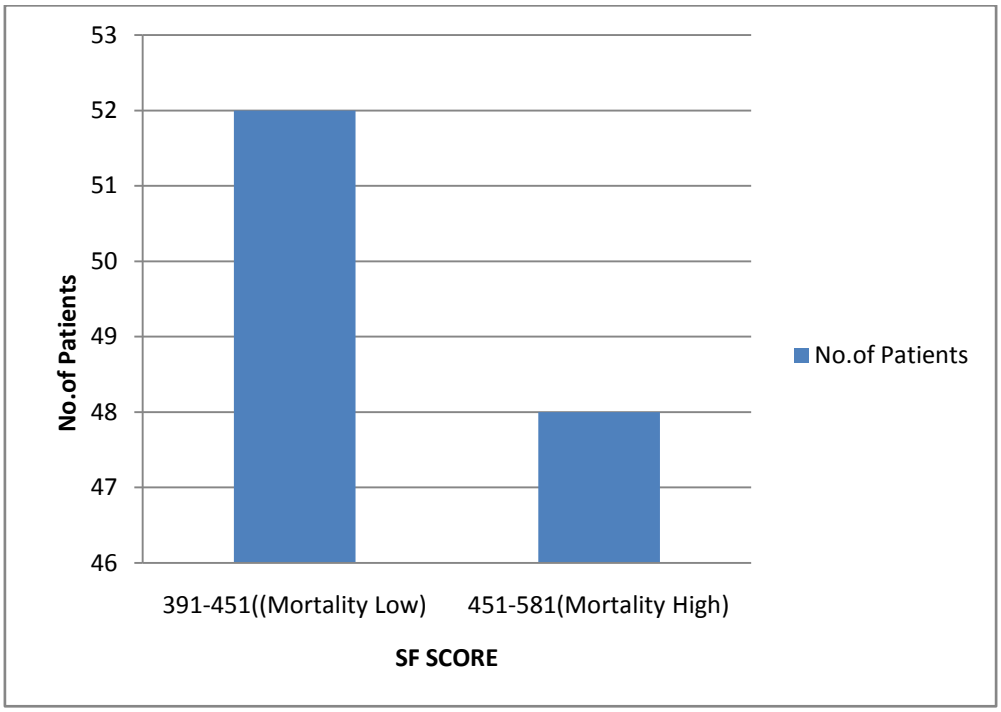


CHART-23

COMPARISON OF SF VALUE AND MORTALITY RATE

We found that even with ripper algorithm SF>298 prone for high mortality. But patients with serum ferritin level more than 451 shows early mortality. So we confirm SF level well correlate and helps us to predict early mortality.



(CHART-24)

ASIF ET AL., H In his work has proved that mortality rate was high if Meld scores above 25.In this work it is proved that even when SF rates are very high the mortality rate also remains very high. Thus it is proved that SF rates and meld score infer the same results.

DISCUSSION

This prospective descriptive and correlation study conducted in GMKMCH, Salem to search wheather serum ferritin level as an independent prognostic marker of hepatic disease.

All the 100 patients enrolled in this study was a known chronic hepatic disease patient most of them presented with one or more of the following signs and symptoms jaundice, ascites, volume overload status, haematemesis, hepatic encephalopathy, hepato renal syndrome.

In our observation we concluded that patients with hepatic encephalopathy orelse hematemesis showing increased ferritin levels in serum and landed up with early mortality within 30 days.

Out of 100 patients 85% are males,15% are females.

Majority of the males are alcoholic around 80%.next to alcohol we found around 28 persons infected by hepatitis B ,22 persons showed anti HCV.

But ferritin levels not correlated with varices. Because not all the patients suffering from the varices developed hematemesis.

Most of the patients presented with reduced urine output with volume overload status noticed that elevated renal parameters and diagnosed as hepatorenal syndrome.HRS highly correlate with ferritin levels.

Criteria for hyperferritenimia according with WHO defined as >300 ng /ML IN males ,>200ng/ml in females.

Since increased ferritin levels caused by multiple factors like NAFLD.steatosis,HCV infections,associated chronic diseases like renal failure,cardiac diseaselike coronary artery disease and cardiomyopathy, cardio renal syndrome we found in chronic liver disease with decompensation serum ferritin levels are elevated.

Zelber-sagi et al[40] done population-based demonstration that NALFLD is one of the important factor for increased ferritin level which indirectly support us oxidative damage to the liver in any form due to variable cause could lead to raised level of ferritin.

By applying ripper analysis we found in our study group >298 of serum ferritin associated with high mortality.

In journal of clinical hepatology Rakhim Maiwall et al conclude that SF predict out come in patients with hepatic decompensation at earlier period.

Nicole M.walker[68] et al analysed that concentrations of SF predicts mortality in patients awaiting for liver transplantation.

Theodora oikonomou et al[67] investigate the role of SF with RDW/MPV and concluded that serum ferritin reflect iron overload status

.

Tan et al studied in 332 patients with CLD verus with out liver disease and found low hepicidin /ferritin ratio.[64]

Wang et al, in his observational analysis found that levels of mean hepcidin was elevated in patients with hepatitis B infection but without cirrhosis.

Bruns et al proved low serum transferring with high ferritin levels acts as an important role of prognostic Marker in ACLF patients [65].

In cirrhotics reduced hepicidin could leads to increased iron deposits in liver and contribute to progressive fibrosis of liver [66] of liver.so one of the negative prognostic marker is serum hepicidin levels which guide us to study the correlation of SF with dcld since we know reduced hepicidin level directly proportionate increased SF level.

Naseer umer et al[67] investigated and concluded Sf level significantly correlate with liver disease severity and independently predict early mortality in decompensated liver .

Natasha Chandok [70]) et al studied the correlation between SF level with NAFLD and concluded that even though hyperferritenemia is common in NAFLD it does not predict the stage of NAFLD.

Neelesh Deshpande [71] et al studied SF as a biochemical marker in Alcoholic liver disease and proved its elevation in patients with decompensated cirrhotics.

Douglas B.Kell explained that serum ferritin is an inflammatory Marker and it actually released from damaged cells.

Maiwall R,et al[69] proved in his study that SF predicts early mortality and also correlated with hepatic decompensation severity .

Finally in our study give conclusion that serum ferritin levels significantly high in non survivors compared with survivors ($p<0.001$).

And there was high correlation between SF level with HRS, HE, Haematemesis, MELD score and predict early mortality on multivariate analysis.

CONCLUSION

Serum ferritin levels well correlated with complications of liver cell failure.

Helps us to predict early mortality in liver disease patients especially with decompensation.

And we conclude that like MELD score, levels of serum ferritin it is independent best prognostic score to predict death and early mortality in dcld patients.

So in future this could be considere one of significant therapeutic and assessment implication in liver disease patients.

SUMMARY

This prospective correlation analytical study was conducted with a sample size of 100 patients presented with complications of decompensated liver disease in GMKMCH, which is one of the tertiary level hospital and we found most of the patients were alcoholic with male predominant.

All patients included in this study had high bilirubin and elevated transaminases. They were found to be not useful in predicting mortality.

High levels of serum ferritin levels observed in patients with advanced liver disease. It is demonstrated to be the marker of necroinflammatory activity and increased iron overload of liver.

In our observation we found serum ferritin was highly accurate in predicting early mortality in patients with decompensated liver cell disease.

At present all of us using MELD score to predict outcome in liver disease, but we observe serum ferritin was superior marker to predict mortality.

Serum ferritin level as an independent prognostic marker in decompensated liver disease appears to be convincing but we have to conduct large prospective multi-center studies should be carried out before being recommended in general and hepatology practice.

BIBLIOGRAPHY

1. McCormick PA , Nolan N . Palpable epigastric liver as a signof cirrhosis. A prospective study.*Eur. J. Gastro. Hepatol.*2004 ;**16** :1331 – 1334 .
2. GinesP , Quintero E , Arroyo V *et al.* Compensated cirrhosis: natural history and prognostic factors . *Hepatology*1987 ;**7** :122 – 128 .
3. Malwai MED j.2012 sep;24(3) :69-71. pmcid : PML 3576830.
4. Furbank RA: Conversion data, normal values, nomograms, and other standards. In Simpson K (ed): Modern Trends in Forensic Medicine. NewYork, Appleton-Century-Crofts, 1967, p 344.
5. Ludwig J: Current Methods of Autopsy Practice. Philadelphia, WB Saunders, 1972.
6. McCuskey RS: The hepatic microvascular system. In Arias IM (ed): The Liver: Biology and Pathobiology, 3rd ed. New York, Raven Press, 1994, p 1089.
7. Davidson VL, Sittman DB: Biochemistry, 3rd ed. Philadelphia, Harwal, 1994.
8. Granner D, Pilkis S: The genes of hepatic glucose metabolism. J Biol Chem 265:10173, 1990.
9. Seifter S, Englard S: Energy metabolism. In Arias IM (ed): The Liver: Biology and Pathobiology, 3rd ed. New York, Raven Press, 1994, p 323.
10. Suttie JW: Vitamin Kdependent carboxylase. Annu Rev Biochem 54:459, 1985.
11. Suttie JW: Recent advances in hepatic vitamin K metabolism and function. Hepatology 7:367, 1987.

12. Furie BC, Furie B: Vitamin Kdependent blood coagulation proteins. In Arias IM (ed): The Liver: Biology and Pathobiology, 3rd ed. New York, Raven Press, 1994, p 1217.

13. Sokol RJ: Fat-soluble vitamins and their importance in patients with cholestatic liver diseases. Gastroenterol Clin North Am 23:673, 1994.

14. Gunshin H,Mackenzie B,Berger UV,Gunshine Y,Romero MF,Boron WF, Nussberger S, gollan JL,Hediger MA.cloning and characterization of a mammalian proton-coupled metal-ion transporter,Nature. 1997;388(6641):482-488.(pub med)

15. Anthony PP, Ishak KG, Nayak NC *et al.* (1978) the morphologyof cirrhosis. Recommendations on definition, nomenclature, and classification by a working group sponsored by the World Health Organization. *J ClinPathol*31(5), 395–414.

16. G. D'Amico, G. Garcia-Tsao and L. Pagliaro, Natural historyand prognostic indicators of survival in cirrhosis: A systematic review of 118 studies, *J Hepatol***44** (2006), 217–231.

17. Garcia-Tsao G, Groszmann RJ, Fisher RL, Conn HO, Atterbury CE, Glickman M. Portalpressure, presence of gastroesophagealvarices and variceal bleeding. Hepatology. 1985;5:419–24.

18. Groszmann RJ, Bosch J, Grace N, Conn HO, Garcia-TsaoG, Navasa M, et al. Hemodynamic events in a prospective randomized trial of propranolol vs placebo in the prevention of the first variceal hemorrhage. Gastroenterology. 1990;99:1401–7.

19. Vorobioff J, Groszmann RJ, Picabea E, Gamen M, Villavicencio R, Bordato J, et al. Prognostic value of hepatic venous pressure

gradient measurements in alcoholic cirrhosis: a 10-year prospective study. Gastroenterology. 1996; 111:701–9.

20. Gines P, Quintero E, Arroyo V. Compensated cirrhosis: natural history and prognosis.Hepatology. 1987;7:122–8.

21. D'Amico G, Morabito A, Pagliaro L, Marubini E. Survival and prognostic indicators incompensated and decompensated cirrhosis. Dig Dis Sci. 1986;31:468–75.

22. Ripoll C, Groszmann R, Garcia-Tsao G, Grace N, Burroughs A, Planas R, et al. Hepaticvenous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. Gastroenterology. 2007; 133: 481– 8.

23. Berzigotti A, Garcia-Tsao G, Bosch J, Grace ND, Burroughs AK, Morillas R, et al. Obesity is an independent risk factor for clinical decompensation in patients with cirrhosis. Hepatology.2011;54: 555–61.

24. Fede G,D"Amico G,Arvaniti V,et al.Renal failure and cirrhosis:a systematic review of mortality and prognosis.J Hepatol. 2012 Apr.56(4) :810-8.(med line) cirrhosis. Hepatology.2011;54:555–61.

25. Planas R, Montoliu S, Ballestè B, Rivera M, Miquel M, Masnou H, et al. Natural history ofpatients hospitalized for management of cirrhotic ascites. ClinGastroenterolHepatol. 2006;4:1385–94.

26. Salerno F, Guevara M, Bernardi M, Moreau R, Wong F, Angeli P, et al. Refractory ascites: pathogenesis, definition and therapy of a severe complication in patients with cirrhosis. Liver Int. 2010;1:937–47.

27. Correia JP, Conn HO: Spontaneous bacterial peritonitis in cirrhosis: Endemic or epidemic. Med Clin North Am 59:963, 1975.

28. Such J, Runyon BA: Spontaneous bacterial peritonitis. Clin Infect Dis 27:669, 1998.

29. Arvaniti V, D'Amico G, Fede G, Mansou P, TsochatzisE, Pleguezuelo M. Infections in patients with cirrhosis increase mortality four- fold and should be used in determining prognosis. Gastroenterology. 2010;139:1246–56.

30. Runyon BA: Albumin infusion for spontaneous bacterial peritonitis. Lancet 354:1838, 1999.

31. Ricart E, Soriano G, Novella MT, et al: Amoxicillin-clavulanic acid versus cefotaxime in the therapy of bacterial infections in cirrhotic patients. JHepatol 32:596, 2000.

32. Navasa M, Follo A, Llovet JM, et al: Randomized, comparative study of oral ofloxacin versus intravenous cefotaxime in spontaneous bacterial peritonitis. Gastroenterology 111:1011, 1996.

33. Terg R, Cobas S, Fassio E, et al: Oral ciprofloxacin after a short course of intravenous ciprofloxacin in the treatment of spontaneous bacterial peritonitis: Results of a multicenter, randomized study. J Hepatol 33:564, 2000.

34. Aparicio JR, Such J, Pascual S, et al: Development of quinolone-resistant strains of *Escherichia coli in stools of patients with cirrhosis* undergoing norfloxacin prophylaxis: Clinical consequences. J Hepatol 31:277, 1999.

35. Runyon BA, McHutchison JG, Antillon MR, et al: Short-course vs long- course antibiotic treatment of spontaneous bacterial peritonitis: A randomized controlled trial of 100 patients. Gastroenterology 100:1737, 1991.

36. Basile AS, Jones EA, Skolnick P: The pathogenesis and treatment of hepatic encephalopathy: Evidence for the involvement of benzodiazepine receptor ligands. Pharm Rev 43:2762, 1991.

37. Zieve L, Doizaki WM, Zieve FJ: Synergism between mercaptans and ammonia or fatty acids in the production of coma: A possible role in the pathogenesis of hepatic coma. J Lab Clin Med 83:1628, 1974.

38. Arroyo V, Gines P, Gerbes AL, et al: Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. Hepatology 23:164176, 1996.

39. Gines P: Diagnosis and treatment of hepatorenal syndrome. Baillieres Best Pract Res Clin Gastroenterol 14:945957, 2000.

40. Spahr L, Fenyves D, NGuyen VV, et al: Improvement of hepatorenal syndrome by transjugular intrahepatic portosystemic shunt. Am J Gastroenterol 90:11691171, 1995.

41. Badalamenti S, Graziani G, Salerno F, Ponticelli C: Hepatorenal syndrome. New perspectives in pathogenesis and treatment. Arch Intern Med 153:19571967, 1993.3

42. Lang F, Gerok W, Haussinger D: New clues to the pathophysiology of hepatorenal failure. Clin Invest Med 71:9397, 1993.

43. Serstè T, Lebrec D, Vallà D, Moreau R. Incidence and characteristics of type 2 hepatorenal syndrome in patients with cirrhosis and refractory ascites. ActaGastroenterol Belg. 2008;71: 9–14.

44. North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices: Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. N Engl J Med 319:983, 1988.

45. Polio J, Groszmann RJ: Hemodynamic factors involved in the development and rupture of esophageal varices: A pathophysiologic approach to treatment. Semin Liver Dis 6:318, 1986.

46. Boyer TD: Portal hypertensive hemorrhage: Pathogenesis and risk factors. Semin Gastrointest Dis 6:125, 1995.

47. Navarro VJ, Garcia-Tsao G: Variceal hemorrhage. Crit Care Clin 11: 391, 1995.

48. Fevery J, Nevens F: Oesophageal varices: Assessment of the risk of bleeding and mortality. J Gastroenterol Hepatol 15:842, 2000.

49. Burroughs AK: The natural history of varices. J Hepatol 17(suppl 2): S10 1993.

50. Brewer TG: Treatment of acute gastroesophageal variceal hemorrhage. Med Clin North Am 77:993, 1993.

51. Pagliaro L, DAmico G, Luca A, et al: Portal hypertension: Diagnosis and treatment. J Hepatol 23:36, 1995.

52. Infante - RivardC ,Esnaola S , Villeneuve J - P *et al.* Clinical and statistical validity of conventional prognostic factors inpredicting short - term survival among cirrhotics . *Hepatology*1987 ;**7** : 660 – 664 .

53. OlthoffKM , Brown RS , Delmonico FL *et al.* Summary report of a national conference: evolving concepts in liver allocation in the MELD and PELD era . *Liver Transpl.*2004 ;**10** : A6 – A22 .

54. Kim WR ,Biggins SW , Kremers WK *et al.* Hyponatremia and mortality among patients on the liver transplant waiting list . *N. Engl. J. Med.* 2008 ; **359** : 1018 – 1026 .

55. Ramond MJ et al.N Engl J Med 1992;326:507-512.

56. Bell H, Skinningsrud A, Raknerud N, et al. Serum ferritinand transferrin saturation in patients with chronic alcoholic and non-alcoholic liver diseases. J Intern Med 1994; 236: 315–22.

57. Fargion S, Mattioli M, Fracanzani AL, et al. Hyperferritinemia, iron overload, and multiple metabolic alterations identify patients at risk for nonalcoholic steatohepatitis. Am J Gastroenterol 2001; 96: 2448– 55.

58. Walker, et al. Serum ferritin concentration predicts mortality in patients awaiting liver transplantation. Hepatology 2010;51:1683-1691.

59. **Nelson JE**, Wilson L, Brunt EM, Yeh MM, Kleiner DE,Unalp-Arida A, Kowdley KV. Relationship between the pattern of hepatic iron deposition and histological severity in nonalcoholic fatty liver disease. *Hepatology*2011; **53**: 448-457

60. **Sorrentino P**, D'Angelo S, Ferbo U, Micheli P, Bracigliano A,Vecchione R. Liver iron excess in patients with hepatocellularcarcinoma developed on non-alcoholic steato-hepatitis. *JHepatol*2009; **50**: 351-357

61. Arroyo V, Gines P, Gerbes AL, Dudley FJ, Gentilini P, Laffi G, et al. Definition and diagnostic criteria of refractory ascites and hepatorenalsyndrome in cirrhosis. Internation Ascites Club. HEPATOLOGY1996;23:164-176.

62. Runyon BA. AASLD practice guideline: management of adult patients with ascites due to cirrhosis. HEPATOLOGY 2004;39:841-856.

63. Zelber-sagi s,Nitzan-kaluski D,Halpern Z,Oren R.NAFLD and hyperinsulinemia are major determinants of serum ferritin levels.J Heptol.2007: 46: 700-707.

64. Tan TC,crawford DH,Franklin ME,et al.The serum hepicidin;ferritin ratio is a potential biomarker for cirrhosis.Liver Int 2012;32;1391- 1399.

65. Bruns T,Nuraldeen R,Mai M,et al.Low serum transferrin correlates with acute on chronic organ failure indicates short term mortality in decompensated cirrhosis. Liver Int 2017;37;232-241.

66. Lunova M,Tratrnad C,strnad P,Nahon P.Reply to ;Hepatic hepicidin expression is decreased in cirrhosis and HCC.J Heptol 2015 ;62;979-980.

67. Theodora oikonomouet al in Ann Gastroenterol.2017;30(2):217-224.

68. Walker, et al. Serum ferritin concentration predicts mortality in patients awaiting liver transplantation. Hepatology 2010;51:1683-1691.

69. Maiwall R et al in J Heptol, 2014 Jul:61 (1);43-50.doi:10.1016/j.jhep.2014.03.027.Epub2014 Mar 26.

70. Natasha chandok,Gerald Minuk et al in division of gastroenterology, multi-organ transplant program,university of western ontario,london.

71. Deshpande,Neelesh,et al.study of biochemical and hemastological markers in alcoholic liver cirrhosis.world journal of nutrition and health 2.2(2014); 24-27.

PROFORMA

Name		IP no		D.O.A	
Age	+	Unit		D.O.Discharge D.O.Death	
Sex		Ward		Duration of stay	
Address			Diagnosis		
Phone No.					
History					
Jaundice			Altered sensorium		
Abdominal Distension			Hematemesis		
Pedal edema			Malena		
Oliguria			Weight loss		
Puffiness of face			Spontaneous bleeding		
Fever			Muscle cramps		
Anorexia			Cough		
fatigue			Breathlessness		
Constipation			Diet		
Diarrhea					
Native medication					
Past h/o jaundice			Tattooing		
Diabetes			Blood transfusion		
Smoking			Drug abuse		
Alcohol Duration Gm/day					
Tuberculosis					
Examination					
HE grade		Clubbing		PR	

Nutrition		Cyanosis		RR	
Height		Parotid swelling		Temp	
Weight		Gynaecomastia		BP Systolic	
BMI		Palmar erythema		Diastolic	
Anaemia		Scrotal swelling		Pulse pressure	
Icterus		Skin changes		Neck veins	
Pedal edema		Abd veins		CVS	
Ascites		Back veins		RS	
Umblical hernia		Caput medusae			
Splenomegaly		Hepatomegaly			
Investigation					
USG Abdomen Liver Size Echoes Ascites Spleen			Endoscopy		
PV Doppler			CXR		
			CRP		
Ascitic fluid culture Colour SAAG Cell count			SERUM FERRITIN		
			Blood culture		
CTP			Urine culture		
MELD		HBsAg		Steroids	
APACHE		HCV		pentoxyfylline	
SOFA		Anti HEV			
HRS		HIV			

Date					
TC					
Hb					
Platlet					
RBS					
Urea					
Creatinine					
Sodium					
Potassium					
Bilurubin TOT					
Direct					
Indirect					
SGOT					
SGPT					
ALP					
Protein					
Albumin					
Globulin					
PT					
INR					
ABG					
Lactate					

REMARKS….

INFORMATION SHEET

We are conducting a study on prospective study of “Serum ferritin as a prognostic marker in a patients with decompensated liver disease” at the department of General medicine, GMKMCH, Salem. The purpose of the study is to know whether serum ferritin predicts early mortality in patients in Decompensated Chronic Liver Disease.

The privacy of the patients in this research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time. Your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the study may be intimated to you at the end of the study period or during the study if anything is found abnormal. This may aid in the management or treatment.

Signature of Investigator……

Signature of participant……

INFORMED CONSENT FORM

Title of the Study:

Serum Ferritin – An Independent Prognostic Marker in predicting Early mortality in decompensated Liver Disease

Name of the Participant:

_____

Name of the Investigator: Dr. s.sangeetha

Name of the Institution : Government Mohan Kumaramangalam Medical College

Documentation of the informed consent

I _____ have read the information of this form (or it had been read to me). I was free to ask any questions and they have been answered. I hereby give my consent to be included as a participant in

Serum Ferritin – An Independent Prognostic Marker in predicting Early mortality in Advanced Liver Disease

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.

Name and signature / thump impression of the participant

Name _____ Signature _____ Date____

Name and signature of impartial witness (required for illiterate patients):

Name _____ Signature _____ Date____

Address and contact number of the impartial witness:

Name and signature of the investigator or his representative obtaining consent:

MASTER CHART

S.NO	SF	AGE	SEX	MELD SCORE	VOLUMEOVER LOAD	URINE OUT PUT	ALTERED SENSORIUM	LFT	HB % (gms)	PLATELETS (L/CU MM)	T.PROTIEN	ALBUMIN	T.BILIRUBIN	D.BILIRUBIN	SGOT	SGPT	S.ALP	HBSAG	ANTI HCV	BT	CT	PT/INR	B.UREA	S.CREATININE	OESOPHAGEAL VARICES	POLYMORPHS
1	412	45	M	30	Y	Y	N	Y	11	1.85	6	3.7	32.6	16.8	48	51	51	N	N	2	9	2.3	46	1.5	Y	N
2	482	48	M	27	Y	Y	N	Y	9.8	1.23	5.9	3.2	12	5.8	26	36	48	N	N	5	12	2.6	36	1.4	Y	Y
3	492	55	F	16	Y	Y	N	Y	8.9	1.92	6.2	4.1	2.9	1.1	36	42	53	N	N	4	15	2	42	1.2	Y	N
4	491	35	M	28	Y	Y	Y	Y	9.1	1.62	6.8	4.2	15.6	9.4	112	132	123	Y	Y	6	10	2.1	68	1.7	Y	N
5	486	38	M	38	Y	Y	N	Y	9.2	1.92	7.1	4.2	11.2	4.8	53	52	48	N	N	2	13	3	32	0.8	Y	N
6	492	41	M	18	Y	Y	N	Y	10.2	2.71	7.2	4.6	2.1	1.5	48	52	51	N	N	3	14	2.5	38	0.9	Y	N
7	452	37	M	20	N	N	N	N	10.8	2.81	6.4	3.9	2.4	1.6	211	162	192	N	N	2	8	2.8	36	1	N	N
8	432	43	M	17	Y	Y	Y	Y	9.4	1.82	6.6	3.8	2.1	1.4	34	38	41	N	N	4	10	2.3	52	1	Y	N
9	421	47	M	22	Y	Y	N	Y	10.2	1.64	6.9	3.9	2.2	1.6	47	38	52	N	N	8	12	3	34	1.2	Y	N
10	498	50	M	19	N	Y	N	N	9.4	1.81	6.9	3.3	2.4	1.8	52	56	58	N	N	7	15	2.6	37	0.9	N	Y
11	462	52	M	28	Y	N	N	N	11.8	1.72	7.1	3.9	14.6	7.2	14	17	52	N	N	3	8	2.9	42	1.3	N	N
12	482	54	M	21	Y	N	N	Y	11.4	1.74	7.4	4.1	19.8	6.8	54	76	80	N	N	2	9	2	40	0.9	Y	N
13	502	56	M	17	N	Y	N	N	10.9	1.92	6.9	4.4	2.4	1.2	12	14	33	Y	N	5	14	2.5	39	0.8	N	N
14	581	58	M	24	Y	Y	N	N	10.4	2.14	6.5	4.8	2.8	1.1	9	12	36	N	N	9	13	2.9	56	1.8	N	N

15	561	52	M	19	Y	Y	N	N	10.5	2.82	6.4	4.2	2.1	1.2	7	14	22	N	N	6	10	2.3	42	1.3	N	N
16	542	53	M	25	Y	Y	N	N	9.4	1.78	6.6	4.3	11.2	6.4	6	9	13	N	N	2	12	2.3	38	1.2	N	Y
17	391	49	M	25	Y	Y	Y	N	9.7	1.71	7.1	4.7	12.8	7.2	7	6	13	N	N	4	9	2.6	36	0.9	N	N
18	402	44	M	18	Y	Y	Y	N	10.2	1.81	7.2	4.8	3.2	1.8	6	9	18	N	N	6	8	2	48	1.2	N	N
19	408	46	M	19	Y	Y	Y	N	10.9	1.82	6.1	4.4	4.2	2.2	14	24	28	N	N	8	9	2.1	46	1.1	N	N
20	466	47	M	45	N	Y	N	Y	9.1	2.12	6.7	4.3	5.2	2.6	12	32	42	N	N	5	12	3	143	10.2	Y	N
21	484	38	M	43	Y	Y	N	Y	9.4	3.12	6.8	3.8	4.1	2.1	14	18	39	N	N	3	15	2.5	239	11.8	Y	N
22	492	41	M	22	Y	N	N	Y	9.2	3.22	6.1	3.7	8.2	3.1	42	48	40	N	N	4	10	2.8	34	0.9	Y	N
23	512	48	M	23	Y	N	N	N	9.8	1.22	6.8	3.8	18.2	6.9	32	36	40	N	N	2	13	2.3	36	0.8	N	N
24	554	62	M	25	Y	Y	N	N	10.2	1.62	7.1	4.2	14.21	5.8	16	23	28	N	N	5	14	3	42	0.6	N	N
25	542	58	M	19	Y	Y	N	N	10.9	2.16	7.4	4.4	2.2	1.32	13	17	21	N	N	8	8	2.6	43	1.1	N	N
26	487	54	M	22	Y	Y	N	N	10.6	2.34	7.1	4.6	3.5	1.82	23	26	29	N	N	9	10	2.9	32	1.2	N	N
27	492	56	M	25	Y	Y	N	Y	9.2	1.91	7.2	4.8	1.1	1	92	72	64	N	N	6	12	2	234	16.2	Y	N
28	501	42	M	34	Y	Y	N	Y	9.4	1.64	7.4	4.1	2.1	1.3	14	18	28	N	N	4	15	2.5	148	5.6	Y	Y
29	502	47	M	23	N	N	N	N	10.1	1.68	6.9	4	8.2	3.8	12	29	42	N	N	2	8	2.9	32	0.8	N	N
30	499	49	M	20	N	Y	N	N	10.9	1.91	6.8	3.7	6.1	2.8	4	7	31	N	N	3	9	2.3	38	0.7	N	N
31	504	44	M	15	N	Y	Y	Y	11.7	2.82	6.2	3.8	3.2	1.2	8	18	72	Y	N	4	14	2.1	36	0.6	Y	N
32	399	46	M	16	Y	Y	Y	Y	11.1	2.91	6.1	3.8	2.3	1.1	17	27	32	N	N	6	13	2.3	42	0.9	Y	N
33	398	45	M	18	Y	N	Y	N	11.6	1.62	6	3.7	1.1	1	31	36	51	N	N	5	10	2.6	39	1.1	N	N
34	392	38	M	35	Y	Y	Y	Y	10.6	1.54	6.9	4.1	1.6	1.3	21	23	28	N	N	9	12	2.9	143	4.9	Y	N
35	401	37	M	15	Y	Y	Y	N	10.9	1.58	7.1	4.2	1.4	1.1	19	21	17	N	N	7	9	2	36	0.9	N	Y
36	404	36	M	18	Y	Y	N	N	11.7	1.64	6.9	4.4	1.8	1.2	42	46	51	N	N	5	8	2.5	42	1.1	N	N

37	418	35	F	20	Y	Y	N	Y	11.8	1.72	6.8	4.1	3.4	1.32	39	42	49	N	N	3	10	3	38	0.8	Y	N
38	464	43	M	18	N	N	N	N	11.4	1.94	7.1	4.6	3.1	1.2	18	12	36	N	N	2	13	2.3	36	0.8	N	N
39	482	48	M	15	N	N	Y	N	10.9	2.21	7.2	4.9	1.6	1.1	42	46	47	N	N	5	14	2	39	1.1	N	N
40	438	50	M	19	Y	Y	N	N	10.6	2.34	6.9	4.2	1.4	1.2	33	26	28	N	N	4	9	2.5	44	1.2	N	N
41	421	52	M	22	y	Y	N	y	10.2	1.2	6.8	3.9	4	2.1	46	52	62	N	N	6.1	8	2.1	42	1.2	y	y
42	491	55	M	30	Y	Y	Y	Y	11	2.1	7.1	4.2	15.6	9.4	112	132	123	Y	Y	6	10	2.1	68	1.7	Y	N
43	486	58	M	28	N	N	N	Y	11.2	1.6	8.1	4.2	11.2	4.8	53	52	48	N	N	2	13	3	32	0.8	Y	N
44	492	60	M	19	Y	Y	Y	Y	9.8	1.8	7.2	4.6	2.1	1.5	48	52	51	N	N	3	14	2.5	38	0.9	Y	N
45	452	52	M	27	Y	Y	N	Y	9.6	2.3	4.2	3.9	2.4	1.6	211	162	192	N	N	2	8	2.8	36	1	N	N
46	432	54	M	19	Y	N	N	Y	10.6	1.12	4.8	3.8	2.1	1.4	34	38	41	N	N	4	10	2.3	52	1	Y	N
47	421	53	M	23	Y	N	N	Y	12	1.6	6.8	3.9	2.2	1.6	47	38	52	N	N	8	12	3	34	1.2	Y	N
48	498	44	M	20	Y	Y	N	N	11.4	1.7	7.2	3.3	2.4	1.8	52	56	58	N	N	7	15	2.6	37	0.9	N	Y
49	462	48	M	31	Y	Y	N	Y	10.4	1.9	5.8	3.9	14.6	7.2	14	17	52	N	N	3	8	2.9	42	1.3	N	N
50	482	49	M	25	Y	Y	Y	N	11	1.6	5.4	4.1	19.8	6.8	54	76	80	N	N	2	9	2	40	0.9	Y	N
51	411	47	M	18	Y	Y	N	Y	11.20%	1.9	7.10%	4.20%	2.90%	2.3	53	48	51	N	N	4	8	2.1	36	1	Y	N
52	501	43	M	41	Y	Y	N	Y	10.10%	1.8	6.70%	4%	15.60%	9.4	148	152	181	N	N	9	18	2.9	194	4.2	Y	N
53	482	42	M	33	Y	Y	Y	Y	11.80%	1.28	7.50%	3.90%	36.60%	17.4	184	158	192	Y	N	9.2	18.5	3	18	1.4	Y	Y
54	402	40	M	28	Y	Y	N	Y	11%	1.80%	7.50%	4.20%	3.10%	2.1	54	58	57	N	N	9	12	3.1	42	1.9	Y	N
55	411	41	F	24	Y	Y	N	Y	11.20%	2.10%	7.20%	4.10%	3.20%	1.2	56	54	55	N	N	8	15	2.8	41	1.8	Y	N
56	408	44	M	19	Y	Y	N	Y	10.80%	1.40%	7.10%	4.20%	4.80%	1.4	58	52	316	N	N	6	12	2.4	38	1.2	Y	N
57	516	46	F	19	Y	Y	Y	Y	11.20%	1.20%	7.10%	4.30%	4.20%	1.2	54	54	320	N	N	7	12	2.1	42	1.4	Y	N
58	511	50	M	21	Y	Y	N	N	10.80%	2.80%	7.30%	4.10%	5.10%	1.3	52	58	311	Y	Y	6	8	2	32	1.8	Y	N
59	512	45	M	24	Y	Y	N	N	11.40%	2.20%	2.40%	4.20%	6.10%	3.2	54	56	312	N	N	8	11	1.9	36	1.9	Y	N

60	518	52	M	26	Y	Y	N	Y	10.40%	2.10%	7.20%	4.80%	7.10%	4.2	58	53	316	Y	Y	9	15	1.8	38	2.1	Y	Y
61	402	53	M	24	Y	Y	N	Y	10.60%	1.90%	7.10%	4.10%	2.80%	5.4	56	56	314	N	N	8	11	1.6	42	1.8	Y	N
62	401	58	M	29	Y	Y	N	Y	11.20%	1.80%	7.80%	4.20%	2.90%	6.6	53	54	141	N	N	6	12	1.9	52	2.4	Y	N
63	409	57	M	20	Y	Y	N	N	11.40%	1.40%	7.20%	4.10%	2.30%	4.8	56	52	146	N	N	7	18	1	52	2.2	Y	N
64	402	49	F	36	Y	Y	Y	Y	10.20%	1.20%	7.10%	4%	2.90%	1.2	53	48	57	Y	N	4	8	3.9	36	4.2	Y	N
65	411	48	M	21	Y	Y	N	Y	11%	1.10%	6.80%	4.10%	12.60%	1.8	55	49	55	Y	Y	9	18	3.1	194	1	Y	N
66	408	57	F	35	Y	Y	N	N	11.20%	1.80%	5.80%	4.20%	11.60%	9.2	54	146	316	Y	Y	9.2	18.5	3.4	18	1.9	Y	Y
67	516	54	F	32	Y	Y	N	N	11%	1.40%	6.70%	4.10%	8.60%	4.8	155	145	320	N	N	9	12	3.5	42	1.8	Y	N
68	511	56	M	26	N	N	N	N	10.80%	1.20%	6.80%	4.80%	7.20%	3.2	154	144	311	N	N	8	15	3.2	41	1.2	Y	N
69	512	58	M	29	N	N	N	N	12%	1.90%	6.90%	4.10%	7.80%	3.4	158	148	312	Y	N	6	12	3.8	38	1.4	Y	N
70	518	38	F	32	Y	Y	N	N	9.90%	2.10%	7.10%	3.80%	4.20%	3.2	159	144	316	N	N	7	12	3.9	42	1.8	Y	N
71	402	40	F	34	Y	Y	Y	Y	9.80%	1.80%	7%	4.20%	2.10%	4.8	158	142	314	Y	Y	6	8	4	32	1.9	Y	N
72	401	39	M	38	Y	Y	Y	Y	11.40%	1.40%	6.40%	4.40%	2.20%	10.2	59	41	141	Y	Y	8	11	4.1	36	2.1	Y	Y
73	409	37	M	30	N	N	N	N	11.80%	1.30%	6.30%	4.30%	2.30%	2.4	53	46	146	N	Y	9	15	3.6	38	1.8	Y	N
74	416	36	F	35	Y	N	N	N	12%	1.40%	6.20%	4.20%	2.80%	5.4	52	48	148	Y	N	8	11	3.3	42	2.4	Y	Y
75	426	35	M	35	Y	Y	N	N	10.20%	1%	6.10%	4.10%	3.10%	6.2	51	44	141	Y	N	6	12	3.6	52	2.2	Y	N
76	481	37	F	44	Y	Y	Y	Y	11.40%	0.90%	5.90%	4.80%	3.20%	9.2	50	44	58	N	N	4	18	3.8	52	4.2	Y	N
77	482	36	M	27	Y	Y	Y	Y	11.60%	0.80%	6.20%	3.90%	4.80%	8.4	51	43	59	N	Y	9	8	3.1	18	1	Y	N
78	413	42	M	35	Y	Y	Y	Y	12%	1.20%	6.40%	3.80%	4.20%	12.2	52	42	60	N	Y	9.2	18	3.2	42	1.9	Y	N
79	417	45	M	39	Y	Y	N	N	10.20%	1.30%	6.60%	4.10%	5.10%	4.1	54	40	70	Y	Y	9	18.5	3.3	41	4.2	Y	N
80	422	41	M	21	Y	Y	N	N	10.80%	1.40%	6.90%	4.20%	6.10%	1.3	56	44	72	Y	N	8	12	3.4	38	1	Y	N
81	423	49	M	29	N	Y	N	N	11%	1.60%	7.20%	3.90%	7.10%	1.8	58	48	74	Y	N	6	15	3.5	42	1.9	Y	Y

82	441	52	M	29	N	N	N	Y	11.20%	1.71%	7.40%	3.90%	2.80%	2.1	54	44	58	N	N	7	12	3.6	32	1.8	Y	N
83	431	51	M	22	Y	Y	Y	Y	9.80%	1.61%	7.10%	3.60%	2.90%	1.8	52	46	56	N	Y	6	12	2.9	36	1.2	Y	N
84	436	53	M	30	Y	Y	Y	Y	9.70%	1.81%	7.20%	3.70%	2.90%	11.4	54	46	54	Y	Y	8	8	2.8	38	1.4	Y	N
85	442	56	M	23	Y	Y	Y	Y	10%	1.78	7.10%	3.80%	2.10%	1.2	58	44	52	Y	N	9	11	2.6	42	1.8	Y	N
86	451	58	M	41	Y	Y	N	Y	10.10%	1.81%	6.90%	3.70%	2.20%	11.3	56	48	54	N	Y	8	15	2.8	52	4.2	Y	Y
87	421	57	M	22	Y	Y	Y	Y	10.20%	1.91%	6.80%	3.60%	2.30%	3.2	53	42	53	Y	Y	6	11	2.7	52	1	N	N
88	426	55	M	30	Y	Y	Y	Y	10.30%	1.94%	6.90%	3.80%	2.40%	5.2	56	46	51	N	N	6	12	2.6	42	1.9	N	N
89	427	53	F	29	Y	Y	Y	Y	10.40%	1.98%	6.80%	3.60%	2.10%	6.4	54	46	58	N	Y	8	18	2.5	32	1.8	N	N
90	481	48	M	25	Y	Y	Y	Y	10.60%	1.99%	6.40%	3.40%	1.90%	7	52	44	112	Y	Y	9	8	2.4	36	1.2	N	N
91	423	49	M	33	Y	Y	Y	N	10%	1.10%	7.10%	3.80%	15.60%	12	56	58	74	Y	N	8	18	3.5	38	1.4	Y	N
92	441	45	M	35	Y	Y	Y	N	11%	0.80%	7.20%	3.70%	12.60%	9.4	58	54	58	N	Y	6	18.5	3.6	42	1.8	Y	N
93	431	44	M	35	Y	Y	Y	N	12%	0.92%	6.70%	3.80%	18.60%	17.4	54	52	56	N	N	4	12	2.9	52	1.9	Y	N
94	436	42	M	28	Y	Y	Y	N	9.80%	11.80%	7.50%	4.20%	17.60%	2.1	52	54	54	N	N	9	15	2.8	52	2.1	Y	N
95	441	41	M	28	Y	Y	Y	Y	9.60%	1.70%	7.80%	4.10%	18.20%	3.8	54	58	52	N	N	9.2	12	2.6	18	1.8	Y	N
96	451	40	M	30	N	N	N	N	9.70%	2.10%	5.80%	4.30%	22%	2.4	58	56	54	Y	Y	9	12	2.8	42	2.4	N	N
97	421	39	M	37	Y	Y	Y	N	9.60%	2.20%	6.80%	4.20%	7.80%	21.2	56	53	53	Y	Y	8	8	2.7	41	2.2	N	N
98	426	38	F	40	Y	Y	Y	N	9.70%	2.10%	7.10%	4.10%	11.60%	11.3	53	56	51	Y	Y	6	11	2.6	38	4.2	Y	N
99	427	47	F	22	N	N	N	N	9.80%	1.92%	6.90%	3.90%	8.60%	4.2	56	54	58	Y	N	7	15	2.5	42	1	Y	N
100	481	57	F	21	Y	Y	Y	Y	9.90%	1.72%	7.50%	3.80%	2.50%	3.2	54	52	112	Y	N	6	11	2.4	32	1.9	Y	N